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OUTCOMES FOR WILMS TUMOR IN CHILDREN IN KINGDOM OF SAUDI ARABIAN ONCOLOGY CENTERS

DR. FAHAD ALAMR
AL-BAHA UNIVERSITY
ASSISTANT PROFESSOR, PEDIATRIC DEPARTMENT, AL-BAHA UNIVERSITY
EMAIL: fahad.a@bu.edu.sa

Abstract
Wilms' tumor (nephroblastoma) is the most common malignant renal tumor in children, accounting for up to 90% of pediatric kidney cancers. In high-income countries, the widespread adoption of multimodal therapy such as surgery, chemotherapy, and radiotherapy has raised survival rates above 90% for localized disease and 70–75% for metastatic cases. Two principal treatment protocols, presented by the Children's Oncology Group (COG) and the International Society of Paediatric Oncology (SIOP), have strengthened these improvements. In Saudi Arabia, although nationwide incidence data are limited, Wilms' tumor constitutes 5–7% of all pediatric cancers and generally presents before five years of age. This review provides a comprehensive overview of Wilms' tumor (nephroblastoma) as managed in Saudi Arabian pediatric oncology centers. It discusses key treatment approaches recommended by international consortia (COG and SIOP), highlights the epidemiology and typical clinical presentation of Wilms' tumor in children, and summarizes findings from multiple Saudi studies. These studies investigate prognostic factors such as hypertension, tumor stage, and histology, as well as the timing of surgical intervention and its impact on relapse and survival. The review demonstrates that, despite some children presenting with advanced-stage disease, outcomes in Saudi Arabia have been steadily improving, approaching international survival rates. However, it emphasizes the importance of early diagnosis, adherence to standardized treatment protocols, and risk-based therapy, particularly regarding patients with hypertension, anaplastic histology, or delayed surgical management.

Keywords: Wilms' tumor, Nephroblastoma, Pediatric oncology, Saudi Arabia, Hypertension, Surgery, Chemotherapy, Outcomes

INTRODUCTION

Wilms' tumor (nephroblastoma) is an embryonal type of renal cancer and one of the most common solid malignant neoplasms in children. It accounts for approximately 90% of all pediatric kidney tumors [1-3]. Despite being a rare disease, significant advancements in risk stratification and treatment approaches have led to significant improvements in survival rates. Through collaborative efforts between pediatric surgeons, oncologists, radiologists, and pathologists, survival rates for localized Wilms' tumor in high-income countries have exceeded 90%, while metastatic cases show survival rates of approximately 75% [4, 5]. The treatment protocol for Wilms' tumor typically includes surgery and chemotherapy, with radiotherapy reserved for high-risk patients. The Children's Oncology Group (COG) and the International Society of Paediatric Oncology (SIOP) have developed treatment strategies that have significantly contributed to improved outcomes. While COG favors primary surgery before adjuvant treatment except in specific cases such as bilateral disease, SIOP advocates for preoperative chemotherapy in all cases except infants younger than six months [3, 6, 7].

Wilms' tumor occurs in approximately 1 in 10,000 children and constitutes around 5% of all childhood cancers [2, 8, 4]. More than 80% of cases are diagnosed before the age of five, with a median age at diagnosis of 3.5 years [9]. Interestingly, Wilms' tumor exhibits slight demographic variations. In Caucasian populations, there is a slight female predominance, whereas in East Asian populations, a higher incidence among boys has been observed, with the peak occurrence in the second year of life [2, 10]. The incidence of Wilms' tumor varies more significantly among different ethnic groups than geographic regions, suggesting a strong genetic component in its etiology. The highest incidence rates have been reported among individuals of African descent, while the lowest rates are observed in Asian populations [10-12]. Wilms' tumor primarily affects a single kidney; however, synchronous bilateral or multifocal tumors are observed in approximately 10% of patients, often presenting at an earlier age [8, 13]. Cases in adolescents and adults are exceedingly rare, accounting for less than 1% of all renal tumors [14].

The majority of Wilms' tumor cases present as an asymptomatic abdominal mass, often first noticed by a family member during bathing or by a healthcare professional observing an enlarged abdomen. In approximately 20-30% of cases, symptoms such as abdominal pain, malaise, and microscopic or macroscopic hematuria occur [15].

Hypertension is a common associated symptom, affecting around 25% of children with Wilms' tumor, most likely due to increased renin activity. In most cases, hypertension resolves after nephrectomy, but persistent or severe hypertension may require further investigation for genetic syndromes such as Denys-Drash syndrome [15]. Atypical presentations are seen in less than 10% of cases and are often due to tumor compression of surrounding organs or vascular invasion. In rare cases, Wilms' tumor can extend into the renal vein or inferior vena cava, occurring in fewer than 4% of patients. These cases may present with symptoms such as ascites, congestive heart failure, and hepatomegaly [15]. Additionally, some children present with acute abdominal symptoms, including a rapidly enlarging abdominal mass, anemia, hypertension, pain, and fever, which may indicate tumor rupture [15, 16]. Paraneoplastic syndromes, though rare, can also be associated with Wilms' tumor. These syndromes include hypercalcemia, erythrocytosis, and acquired von Willebrand disease, which result from tumor production of hormonal substances [15, 17].

The diagnostic approach to Wilms' tumor begins with imaging studies. Abdominal ultrasound is the initial modality of choice to confirm the presence of an intrarenal mass, assess tumor extension, and evaluate the contralateral kidney. Ultrasound also helps determine vascular invasion, including extension into the inferior vena cava or liver metastases. It is essential to rule out associated genitourinary malformations and confirm the presence of a functional contralateral kidney [15, 16, 18]. Following ultrasound, cross-sectional imaging with computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis is standard practice for further tumor characterization. MRI is particularly useful for patients with suspected bilateral Wilms' tumor as it reduces radiation exposure. Advanced imaging techniques such as Apparent Diffusion Coefficient (ADC) mapping can provide additional biological insights into tumor behavior [19]. The lungs are the most common site of metastasis, occurring in 10-20% of children at diagnosis. Traditionally, chest radiography has been used to detect lung metastases, but chest CT is increasingly preferred for its higher sensitivity. However, there is ongoing debate on whether small lung lesions detected only by CT should be treated aggressively [20]. Intravenous tumor extension is observed in approximately 11% of Wilms' tumor cases, with thrombus involvement of the inferior vena cava occurring in around 4%. In suspected cases of intracardiac extension, echocardiography is recommended to assess tumor spread to the heart [15].

Wilms' tumor management typically follows one of two main strategies: the Children's Oncology Group (COG) protocol or the International Society of Paediatric Oncology (SIOP) protocol [3, 6, 7]. The COG approach, used predominantly in North America, favors immediate nephrectomy to achieve precise staging and histological evaluation prior to chemotherapy, but this can increase the risk of tumor spillage and subsequent need for flank radiotherapy if Stage III disease is identified [4]. By contrast, SIOP protocols, applied in Europe and the UK, recommend four to six weeks of preoperative chemotherapy to shrink the tumor and minimize surgical complications, with randomized trials showing no significant difference in event-free or overall survival between the two approaches [4, 5, 21, 22]. SIOP advises immediate nephrectomy only in infants under six months, given the higher likelihood of benign renal tumors and non-Wilms' malignancies in this age group [16, 23], whereas older children receive chemotherapy first and are then assessed histologically, with tumors exhibiting persistent blastema classified as high risk [16, 23]. Despite differences in timing, both approaches achieve comparable long-term survival of around 90% for localized tumors and above 70% for metastatic disease [4, 6, 7, 21].

Surgical management is central to therapy, typically involving transperitoneal radical nephrectomy for unilateral disease and thorough lymph node sampling, given that imaging alone can miss nodal involvement in over 30% of cases [1, 9]. Positive nodal findings necessitate para-aortic radiotherapy to lower recurrence risk [1, 3, 6]. Nephron-sparing surgery is reserved for bilateral Wilms' tumor (Stage V) or syndromic presentations (e.g., Denys-Drash) to preserve renal function, though it is generally avoided in unilateral cases due to higher recurrence rates [7, 24]. Postoperative complications include intraoperative bleeding and small bowel obstruction (>5% incidence), while preoperative chemotherapy can facilitate renal-sparing procedures in bilateral disease by reducing tumor volume [9].

Chemotherapy and radiotherapy regimens differ slightly between COG, which escalates treatment postoperatively based on stage and histology [4, 5], and SIOP, which uses preoperative vincristine plus actinomycin D (and doxorubicin for metastatic cases) [4]. Both strategies acknowledge the utility of preoperative therapy for large or unresectable tumors, bilateral disease, and cases with tumor extension into the inferior vena cava or right atrium [1, 4], and whole-lung radiotherapy is considered for Stage IV disease if pulmonary metastases remain after chemotherapy [16, 21]. Biopsy practices vary, as COG automatically upgrades tumors to Stage III if biopsied, mandating radiotherapy, whereas SIOP in the UK previously employed needle biopsy in non-metastatic tumors but no longer routinely does so due to concerns about tract seeding [21, 25]. In resource-limited settings, late-stage presentation (Stage III/IV) is common, and the SIOP method is often favored, as preoperative chemotherapy reduces surgical risks when advanced perioperative resources are limited [7, 25, 26]. Long-term, a key challenge is balancing curative treatment with the need to preserve renal function, since bilateral disease carries up to a 15% risk of end-stage renal disease (ESRD) within 15 years post-treatment [24].

OUTCOMES FOR WILMS' TUMOR IN CHILDREN IN SAUDI ARABIAN ONCOLOGY CENTERS

Precise nationwide incidence figures for Wilms' tumor (WT) in Saudi Arabia are not extensively reported in the literature; however, available data suggest that WT is the most common malignant renal tumor in Saudi children and accounts for approximately 5–7% of all pediatric cancers in the Kingdom [27]. An older single-institution series by Farsi et al. noted Wilms' tumor as a frequent pediatric renal malignancy at King Abdulaziz University Hospital in Jeddah, reporting its prominence among childhood solid tumors in the region [37]. Similarly, retrospective reviews from major tertiary centers (e.g., King Faisal Specialist Hospital & Research Centre and Princess Noorah Oncology Center) have consistently described WT as comprising a significant portion of pediatric oncology caseloads [28, 30, 35]. In general, the age at diagnosis and clinical presentations in Saudi Arabia reflect international trends, with most cases occurring in children under five years of age and presenting with an abdominal mass [27]. Despite some patients appearing at advanced stages, particularly in resource-limited or peripheral settings, multicenter reports suggest that outcomes in Saudi Arabia have steadily improved over the past two decades [28, 34].

Jastaniah et al. analyzed 85 pediatric WT patients (71 with complete data) diagnosed between 2000 and 2013 at Princess Noorah Oncology Center, King Abdulaziz Medical City in Jeddah [28]. Their primary focus was the prognostic significance of hypertension (HTN) at diagnosis. The investigators found that 35.2% of patients were hypertensive, and these patients exhibited markedly worse survival compared to normotensive children. Specifically, the hypertensive group had a five-year overall survival (OS) of 67.1% versus 89.6% in the normotensive group ($p = 0.009$), and a five-year progression-free survival (PFS) of 53.4% versus 79.1% ($p = 0.007$). Hypertension was identified as an independent predictor of poor OS ($p = 0.004$) and PFS ($p = 0.010$) on multivariate analysis, along with local tumor stage and histopathology. Notably, hypertensive patients with localized Stage I/II disease had significantly worse OS (81.6%) compared to normotensive counterparts (100%, $p = 0.032$), suggesting that hypertension may reflect more aggressive tumor biology or treatment resistance. They concluded that routine assessment of blood pressure and consideration of hypertension in risk stratification could improve outcomes for high-risk pediatric WT patients. Moreover, Al Mulhim examined the clinical characteristics and outcomes of 18 pediatric WT cases treated at King Fahd Hospital of the University in Alkhobar between 1985 and 1994 [29]. The median age at diagnosis was 2.5 years, and the cohort comprised eight males and ten females. Stage distribution included 11% at Stage I, 33% at Stage II, 44% at Stage III, and 6% each at Stage IV and V. Favorable histology was observed in 94.5% of patients, with anaplastic histology noted in 5.5%. All children presented with an abdominal mass; other symptoms included abdominal pain (27.8%), hematuria (16.7%), and hypertension (11%). Nephrectomy was performed in all cases, followed by chemotherapy and, when indicated, radiotherapy according to National Wilms' Tumor Study (NWTS) II and III guidelines. Overall disease-free survival was 88.8%, and two patients died—one from local recurrence with metastasis and another due to progressive disease. Survival for Stage I and II disease reached 100%, while treatment-related toxicity was minimal.

In another research, Khattab et al. investigated the influence of surgical timing on local recurrence and overall survival in 58 pediatric WT patients at Princess Noorah Oncology Center, National Guard Hospital, in Jeddah, treated between 1986 and 2004 [30]. Patients were managed with either immediate nephrectomy or delayed nephrectomy (following biopsy and preoperative chemotherapy) in cases of bilateral, metastatic, or unresectable disease. Of six bilateral WT cases, none experienced relapse, whereas three of six patients with unfavorable histology relapsed and died. Among the 46 patients with favorable histology, the overall five-year survival was $76.6\% \pm 6.5\%$. However, local recurrence rates differed substantially: 6.4% in the immediate nephrectomy group compared to 44% in the delayed group ($p = 0.003$). The five-year survival was also significantly better following immediate nephrectomy ($86.7\% \pm 6.2\%$) than delayed nephrectomy ($52.2\% \pm 14.3\%$, $p = 0.023$). Prolonged delay (beyond 56 days) appeared to increase the likelihood of relapse. The investigators concluded that prompt surgical management is necessary for optimal outcomes, as delays in local therapy adversely affect survival (Khattab et al., 2009).

Furthermore, Ahmad et al. conducted a retrospective review at King Abdullah Specialist Children's Hospital in Riyadh, focusing on 39 pediatric Wilms' tumor patients diagnosed between 2001 and 2015, with 36 ultimately meeting inclusion criteria [31]. The median age at diagnosis was three years, and 44% were male. Stage distribution showed that 28% had Stage I disease, 6% had Stage II, 36% had Stage III, 22% had Stage IV, and 8% had Stage V disease, with pulmonary metastasis being the most prevalent pattern of spread. Upfront nephrectomy was performed in 86% of patients, whereas 14% underwent only a biopsy procedure, including all cases of Stage V disease. Histopathological examination revealed favorable histology in 83%, focal anaplasia in 8%, diffuse anaplasia in 6%, and one rhabdoid tumor case. Relapse occurred in 25% of patients and correlated strongly with anaplasia ($p = 0.0003$). The overall five-year survival rate was 83%, and event-free survival was 74%, which is

comparable to outcomes in several middle-income countries but somewhat lower than rates in high-income nations. Patients with Stage I, II, and V disease experienced 100% five-year survival, whereas those with Stage III and IV disease had survival rates of 68% and 72%, respectively. Six patients died of progressive disease, all within two years of diagnosis, and relapsed cases had an overall survival of 33%, which falls on the lower end of reported ranges for relapsed Wilms' tumor. Two survivors developed secondary malignancies, highlighting the importance of long-term surveillance. They concluded that while outcomes at their institution generally align with other developing regions, incorporating tumor genetics-based risk stratification could further enhance treatment personalization and improve survival to match those observed in high-income countries.

Another study by Khattab et al. investigated the outcomes in 35 pediatric Wilms' tumor cases treated at a single institution in the Western Region of Saudi Arabia between 1986 and 2000 [32]. They compared children who received preoperative chemotherapy with those who underwent early nephrectomy to determine the impact of treatment timing on local recurrence and survival. Stage distribution included 4 patients with Stage I disease, 8 with Stage II, 14 with Stage III, 4 with Stage IV, and 5 with Stage V. Most patients (31) had favorable histology, whereas 4 had unfavorable histology (anaplastic Wilms' tumor, clear cell sarcoma, or rhabdoid tumor). Local recurrence developed in 8 patients (23%). Of the 13 children who received preoperative chemotherapy, 6 (46%) experienced local recurrence, compared to only 2 of 19 (10%) who underwent early nephrectomy. Survival varied greatly by histological subtype; those with favorable histology achieved an 80% survival rate, whereas unfavorable histology cases demonstrated only 25% survival. Nearly all patients with local recurrence died from disease progression, except for one who initially presented with lung metastases rather than local failure. They attributed high local recurrence rates to factors including unfavorable histology, advanced tumor stage, inoperability at presentation, and treatment delays. The researchers recommended earlier surgical intervention or earlier irradiation in inoperable cases to reduce local recurrence and improve overall survival. Additionally, Altwaeel et al. presented two rare cases of Wilms' tumor with intracardiac extension managed at King Abdulaziz Medical City in Riyadh, reporting the complex perioperative approach required in such advanced clinical scenarios [33]. The first case involved a 32-month-old female with Stage IV, left-sided disease and tumor thrombus extending into the right atrium. Neoadjuvant chemotherapy produced minimal tumor response, leading to a combined sternotomy and laparotomy for radical nephrectomy and intracardiac tumor resection under cardiopulmonary bypass. The perioperative course was uneventful, although the patient required antihypertensive therapy postoperatively. The second case was a 13-month-old male with right-sided Stage IV WT, inferior vena cava involvement, and intracardiac extension into the right atrium and ventricle. Following neoadjuvant chemotherapy, a combined urology and cardiac procedure was performed with complete resection, also under cardiopulmonary bypass. Postoperative anticoagulation was used to prevent thrombotic complications. Both cases demonstrated the importance of a multidisciplinary team, including pediatric oncology, cardiac surgery, anesthesiology, and intensive care in achieving favorable outcomes. These outcomes show the application of intraoperative transesophageal echocardiography (TEE) for precise tumor localization and completeness of resection, as well as the need for careful management of potential complications such as thromboembolism, dysrhythmia, and hemorrhage.

Further, Omar et al. conducted a retrospective review of 22 pediatric Wilms' tumor cases at King Fahad Specialist Hospital in Dammam, covering diagnoses from 2011 to 2016 [34]. The median age at diagnosis was 37.2 months, and 59.5% of the cohort were female. Stage III was most common at 31.8%, followed by Stage I at 27.3%, while the majority of tumors (70%) exhibited favorable histology, 10% showed anaplastic features, and 20% demonstrated mixed pathology. The relapse rate was 18.2%, and the mortality rate reached 9%, both consistent with international statistics. An event-free survival (EFS) of 80% and an overall survival (OS) of 90% closely mirrored outcomes reported by established consortia such as the National Wilms Tumor Study Group (NWTS-5). Notably, despite a relatively higher proportion of Stage III presentations, the observed relapse and progression rates remained comparable to global data, suggesting that treatment protocols at this center effectively managed more advanced disease. These outcomes highlighted the importance of standardized, protocol-driven care and a multidisciplinary approach in achieving survival rates similar to those found in Western countries.

Moreover, in another retrospective study at King Faisal Specialist Hospital & Research Centre (KFSH&RC), Al Fawaz et al. analyzed 144 evaluable pediatric Wilms' tumor (WT) cases with favorable histology diagnosed between 1980 and 2001, excluding bilateral cases [35]. Diagnosis was established primarily through upfront nephrectomy in 88 cases (61.1%), followed by fine-needle aspiration in 45 (31.3%), and open biopsy in 11 (7.6%). Stage distribution included Stage I in 30.6% of patients, Stage II in 16%, Stage III in 32.6%, and Stage IV in 20.8%. All patients received multimodal treatment—surgery, chemotherapy, and radiotherapy—in line with National Wilms' Tumor Study (NWTS) protocols. First-line therapy resulted in 119 complete remissions, while 7 patients had progressive disease, 11 died during therapy, and 7 were lost to follow-up. Of those who achieved remission, 24 relapsed off treatment and required second-line interventions. After a median follow-up of 35 months (range: 0.1–170 months), the five-year overall survival (OS) was 85% and the event-free survival (EFS) was 58%. Stage-specific survival outcomes favored early stages, with Stage I cases reaching 95% OS and 83%

EFS, whereas Stage IV patients achieved 65% OS and only 24% EFS. The relapse or progression rate (22%) remained comparable to NWTS-3 data, albeit in a cohort that presented with a higher percentage of advanced disease. Al Fawaz et al. concluded that despite later tumor presentation, overall survival rates at their institution resembled those in Western countries, reinforcing the effectiveness of multidisciplinary therapy. Nevertheless, they highlighted that improving EFS in Saudi patients would require earlier diagnosis and intervention.

Furthermore, Sabbah et al. described a specialized approach for five Saudi children, aged between 2 and 6 years, who presented with far advanced Wilms' tumors at King Faisal Specialist Hospital & Research Centre [36]. These cases were designated "Stage S" because of massive tumor burden, widespread disease, and severe systemic complications—including malnutrition, pulmonary compromise, and infection—that rendered the patients unfit for surgery under conventional NWTS Group protocols. The researchers introduced an optimized regimen (KFSH 79-3) incorporating preoperative chemotherapy with vincristine, actinomycin D, and doxorubicin, combined with radiotherapy (2000–3600 rads) and total parenteral nutrition to optimize the children's conditions. After two to three months of preoperative treatment, all tumors underwent sufficient regression to permit successful nephrectomy. Two children remained disease-free, two died of unrelated gastroenteritis while in remission, and one developed pulmonary metastases and received a modified regimen. Sabbah et al. concluded that intensive preoperative therapy, including nutritional and radiologic support substantially enhanced operability and survival prospects in this severely debilitated subgroup, advocating individualized protocols for patients who cannot immediately tolerate surgical intervention. Additionally, Farsi et al. reviewed 12 pediatric Wilms' tumor patients at King Abdulaziz University Hospital in Jeddah over a four-year span (1983–1987) to assess clinical presentation and outcomes in comparison with Western data [37]. The mean age at diagnosis was 25 months, and the majority of patients presented with Stage II or III disease. An abdominal mass was the most frequent presenting sign, detected in 66% of cases, followed by abdominal pain and hematuria. Hypertension was notably high at 50%, exceeding the prevalence typically reported in Western cohorts. Radical nephrectomy was performed on most patients except one, who required preoperative vincristine due to a large tumor mass. Two children had diffuse anaplasia, and 41% had lymph node involvement, exceeding the 17.8% rate reported in NWTS data. Postoperative chemotherapy (actinomycin D, vincristine, and doxorubicin) and radiotherapy were administered based on tumor stage. The overall survival rate reached 81%, comparable to international figures despite the higher rates of advanced disease. One patient with unfavorable histology succumbed to metastatic disease, showing the influence of anaplasia on prognosis. Farsi et al. emphasized the importance of a national collaborative oncology network in Saudi Arabia to standardize treatment approaches, facilitate clinical trials, and ultimately enhance outcomes.

Moreover, Sackey et al. documented a case of congenital hemihypertrophy with concurrent Wilms' tumor in a 3-month-old girl treated at King Faisal Specialist Hospital [38]. Clinical evaluation and computed tomography confirmed total right hemihypertrophy involving the face, upper limb, lower limb, and thorax, without aniridia or genitourinary anomalies. The child's Wilms' tumor exhibited favorable histology, and she was managed with vincristine and actinomycin D, remaining disease-free four months after diagnosis. They reported that among 32 consecutive Wilms' tumor cases at their hospital, this was the only instance of hemihypertrophy, consistent with a 3% incidence. They stressed the elevated risk of abdominal malignancies—including Wilms' tumor, adrenal tumors, hepatoblastoma, and neuroblastoma—in patients with hemihypertrophy. Routine abdominal imaging and careful follow-up were recommended to detect malignancies at an early, more treatable stage. In a separate report, Sackey et al. described a two-year-old girl presenting with bilateral aniridia and Wilms' tumor (Aniridia-Wilms' Tumor Association), one of 54 WT cases at King Faisal Specialist Hospital [39]. Cytogenetic analysis revealed an interstitial deletion on chromosome 11 (11p13p15.1), a genetic defect commonly linked to AWTA. The patient underwent left nephrectomy followed by chemotherapy (actinomycin D, vincristine, and adriamycin). A subsequent lesion in the right kidney responded to intensified chemotherapy, and she remained tumor-free 29 months post-diagnosis. These outcomes show that children with sporadic aniridia carry a significantly higher risk of Wilms' tumor compared to the general population, emphasizing the necessity for thorough cytogenetic investigation, regular ultrasound surveillance, and prolonged follow-up until at least 10 years of age to detect bilateral or metachronous disease early.

The studies examined provide a comprehensive picture of Wilms' tumor (WT) outcomes in children treated at various oncology centers across Saudi Arabia. The outcomes revealed both encouraging trends in overall survival and important prognostic factors that may shape future treatment approaches. One notable finding, highlighted by Jastaniah et al., is the independent prognostic value of hypertension in pediatric WT [28]. The worse overall and progression-free survival among hypertensive patients suggests that blood pressure status might signify more aggressive tumor behavior or resistance to therapy. Particularly striking is the observation that hypertensive patients with Stage I/II disease fared significantly worse than their normotensive counterparts, highlighting the potential need for closer monitoring and more aggressive treatment strategies in this subset. Moreover, the high curability of WT in Saudi Arabia, observed by Al Mulhim and others, is in line with international data, especially for early-stage disease and favorable histology [29]. This finding indicates the importance of prompt diagnosis and adherence to established protocols such as multimodal regimens that incorporate surgery, chemotherapy, and

where appropriate, radiotherapy. At the same time, these results draw attention to the fact that stage at presentation and histological subtype (particularly anaplasia) continue to be critical determinants of long-term survival. Accordingly, centers that adhere to standardized staging and treatment protocols, such as the National Wilms' Tumor Study (NWTS) guidelines, have reported survival outcomes comparable to—or only slightly below—those in high-income countries.

Notably, treatment timing also appears to be a key factor, as demonstrated by Khattab et al., who reported significantly higher local recurrence and poorer survival among patients subjected to delayed nephrectomy [30]. Delays beyond 56 days from diagnosis appeared to further increase relapse risk, highlighting the importance of prompt local therapy when feasible. Although preoperative chemotherapy can downstage bilateral, metastatic, or otherwise inoperable tumors, these data indicate that unnecessary postponements may compromise outcomes. Similar observations were also reported from the additional studies. Ahmad et al. found that anaplasia and advanced stage remain significant predictors of relapse and mortality, highlighting the need for tumor biology-based risk stratification [31]. Meanwhile, Khattab and colleagues, in a separate single-institution study, observed high local recurrence rates in patients with advanced tumor stage, unfavorable histology, and treatment delays [32]. Likewise, Omar et al. highlighted the value of strict adherence to protocol-driven treatment, showing that even with a high proportion of Stage III presentations, survival rates can approximate those seen in Western centers [34]. These findings collectively show the centrality of a disciplined, multidisciplinary approach, including oncologists, surgeons, radiologists, and critical care teams to optimize patient outcomes.

Furthermore, complex cases involving intracardiac extension or poor patient fitness at presentation, as illustrated by Altwaeel et al. and earlier data from Sabbah et al., show the necessity for individualized [33, 36], often intensive management strategies. Such approaches may include neoadjuvant chemotherapy, radiotherapy, nutritional support, and in rare scenarios, cardiopulmonary bypass for safe tumor resection. Although these situations are uncommon, they demonstrate that coordinated teamwork can yield favorable results, even under challenging circumstances. In conclusion, these studies converge on several key recommendations for improving WT outcomes. Early and accurate staging, careful monitoring for high-risk features such as hypertension or anaplasia, timely surgical intervention, and strict adherence to established protocols all contribute to promising survival rates. Areas that warrant further development include the incorporation of tumor genetics into routine risk stratification, greater focus on relapsed disease management, and continued efforts to detect WT in its earliest stages. In future, large-scale, prospective, multicenter collaborations would help confirm these findings and further refine treatment pathways.

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