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Challenges to bridging the survival gap in Wilms tumour: insights from a 24-year experience from a tertiary cancer care centre in Southern India

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Abstract

Wilms tumour (WT) is one of the most common paediatric renal malignancies. While the overall survival (OS) has improved above 90% in high-income countries, the outcomes remain inferior in low- and middle-income countries (LMICs) due to the healthcare system and socioeconomic barriers. This study aimed to document the demographic profile, clinical features and treatment patterns, and to evaluate the survival outcomes of children with WT managed in our institute. We retrospectively analysed patients diagnosed as WT between January 2000 and December 2023 at the Paediatric Oncology Unit of a tertiary care cancer centre in Southern India. Descriptive statistics were used to summarise the demographic profile, clinical features and treatment patterns. Event-free survival (EFS) and OS were estimated using Kaplan–Meier methods. Sixty-nine children were diagnosed with WT at our centre during the study period. The median age at diagnosis was 34 months (range: 8–159 months), with a slight male predominance (M:F ratio 1.22:1). Seventeen (25%) children without any image-defined high-risk factors underwent upfront nephrectomy while the remaining 52 (75%) children received preoperative chemotherapy followed by delayed nephrectomy. The stage distribution was as follows: Stage I–24 (35%); Stage II–15 (22%); Stage III–13 (19%); Stage 4–13 (19%); Stage 5–3 (3.5%); and Unknown–1 (1.5%). With a median follow-up of 68.5 months, the 5-year EFS and OS rates of our study cohort were 69% (95% confidence interval (CI): 56%–78%) and 78% (95% CI: 65%–87%), respectively. The most common causes of treatment failure were relapse (22%) and treatment abandonment (11%). Multivariate analysis revealed that advanced stage and upfront nephrectomy were independent predictors of inferior survival. Survival outcomes for WT in LMICs remain inferior despite multidisciplinary management. A hybrid approach – tailoring surgical timing to individualised risk – appears pragmatic. Bridging the survival gap requires addressing socioeconomic barriers and strengthening multidisciplinary care.

Keywords: *child, kidney neoplasm, Wilms tumour, nephroblastoma*

Introduction

Paediatric renal tumours constitute 3.2%–11.1% of all childhood cancers globally [1]. Wilms tumour (WT) is the most common paediatric renal tumour [2]. Major collaborative

Research

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ecancer 2026, **20**:2217
https://doi.org/10.3332/ecancer.2026.2217

Published: 22/09/2026
Received: 05/05/2026

Publication costs for this article were supported by *e*cancer (UK Charity number 1176307).

groups, including the National Wilms Tumor Study Group/Children's Oncology Group (NWTS/COG), the Société Internationale d'Oncologie Pédiatrique (SIOP) and the United Kingdom Children's Cancer Study Group have played a pivotal role in advancing the understanding and management of WT [3]. As a result, the overall 3- to 5-year survival rates of WT now exceed 90% in high-income countries (HICs) [4].

The success story of WT stems from intensive multimodal treatment strategies, including surgery, chemotherapy and radiotherapy [3, 4]. Although such multimodal therapy is feasible in India, the reported overall survival (OS) rates for WT vary widely, ranging from 48% to 91%. This is due to challenges such as delayed presentation and diagnosis leading to advanced disease stage at diagnosis, treatment-related mortality, treatment abandonment, lack of uniform treatment guidelines, limited access to surgical and pathological expertise that hinders accurate staging and risk stratification and delays in the timely administration of radiotherapy [5, 6].

Since WT is one of the six index cancers identified by the World Health Organization (WHO) – Global Initiative for Childhood Cancer, efforts to bridge the survival gap between HICs and low- and middle-income countries (LMICs) require a clear understanding of the current survival rates, treatment patterns and barriers to care [7]. Although a few recent studies from India have reported the outcomes of WT, considerable heterogeneity in treatment practices and patient characteristics persists. This study aims to document our centre's experience in managing children with WT [5, 6, 8, 9].

Methods

Study design, setting and participants

We retrospectively analysed patients evaluated for renal tumours between January 2000 and December 2023 at the Paediatric Oncology Unit, of a tertiary care cancer centre in Southern India. Our centre will be classified as setting 3 according to the SIOP – Paediatric Oncology in Developing Countries definition of resource settings necessary for diagnosing and managing children with cancer [10, 11]. This study included patients under 18 years of age with confirmed WT (typical clinical and radiological features with histopathological diagnosis of WT on biopsy and/or nephrectomy specimen) as well as probable WT (typical clinical and radiological features without histopathological diagnosis of WT on biopsy and/or nephrectomy specimen). We also included patients who had undergone upfront nephrectomy elsewhere, provided that histopathological diagnosis and staging were confirmed at our centre and essential surgical details (including information on tumour spill/rupture and lymph nodal sampling) were available. Our objective was to evaluate the demographic profiles, clinical features, treatment and survival outcomes of children with WTs managed in our unit. Prior approval and clearance were obtained from the institutional ethics committee for data analysis and publication (Ref: IEC/2025/April 16). All procedures performed in our study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Data collection

Clinical characteristics, including age, gender, presenting symptoms, duration of symptoms and sites of involvement, were abstracted from medical records. We also retrieved reports of haematological and biochemical investigations, imaging studies (X-ray, ultrasonography and computerised tomography (CT) scan) and histopathological studies from the medical records. Treatment details (chemotherapy, surgery and radiotherapy) were gathered from patients' records. All patients in the study were followed up by medical record review until March 2025.

Initial diagnosis and evaluation

All patients presenting with a renal mass underwent contrast-enhanced CT (CECT) of the abdomen and pelvis. The clinical features and imaging characteristics were utilised to formulate a presumptive diagnosis of WT. The initial staging investigations for a child with a presumptive diagnosis of WT included chest X-ray and CT chest. Patients with characteristic lung or liver lesions were classified as having metastatic disease, whereas those without such lesions were categorised as having localised disease.

Treatment

The treatment decisions of the study participants were taken after discussion in a multidisciplinary tumour board. The resources for treatment of WT and the treatment protocol have evolved in the author's unit during the study period; therefore, the treatment of the patients enrolled in the study is heterogeneous. The baseline CT images of the patients with presumptive diagnosis of WT were carefully evaluated for the image-defined high-risk features, namely: 1) large renal tumour crossing the midline, 2) primary tumour/lymph nodal mass infiltrating the surrounding viscera/major vessels that may warrant a multiorgan resection, 3) inferior vena cava thrombus, 4) metastatic disease and 5) bilateral WT, unilateral WT with bilateral predisposition, or WT arising from a solitary kidney/horseshoe kidney. The children presenting with any of these high-risk features were deemed unsuitable for upfront nephrectomy and were administered preoperative chemotherapy followed by delayed nephrectomy. The patients without these features underwent upfront nephrectomy.

Upfront nephrectomy (NWTS/COG approach)

All patients deemed resectable upfront underwent open or robotic-assisted radical nephroureterectomy with standard-template retroperitoneal lymph node dissection [12]. The surgical specimens underwent histopathological examination for staging and histological subtyping, according to the NWTS/COG staging system and COG histological classification criteria, respectively [4, 13, 14] (Supplementary Tables 1 and 2). None of the patients were tested for loss of heterozygosity at 1p and 16q. Based on the assigned stage and histology, patients received adjuvant therapy, as per the NWTS-5 study protocol [15, 16].

Preoperative chemotherapy followed by delayed nephrectomy (SIOP approach)

All the patients with high-risk features precluding upfront resection would receive 4–6 weeks of preoperative chemotherapy comprising vincristine and actinomycin D with/without anthracycline (doxorubicin/epirubicin) [4, 14]. Image-guided percutaneous biopsy was reserved only for those with atypical clinical and radiological features to confirm the diagnosis of WT. Response to preoperative chemotherapy at the primary and metastatic sites, was assessed using CECT – chest, abdomen and pelvis [17].

Following preoperative chemotherapy, patients underwent open or robotic-assisted radical nephroureterectomy with standard-template retroperitoneal lymph node dissection. Nephron-sparing surgery was reserved for bilateral WT, unilateral WT with bilateral predisposition, or WT arising from a solitary kidney/horseshoe kidney [12]. The surgical specimens were examined histopathologically for stage, extent of necrosis and histological subtype. Staging was performed according to the SIOP staging system, while histological classification was based on the SIOP criteria [4, 13, 14] (Supplementary Tables 1 and 2). Based on the final stage, histological risk group and metastatic response, patients received adjuvant therapy according to the SIOP-9/SIOP-93 protocols (before 2010) and the SIOP 2001 protocol (after 2010) [18–20].

Data management and statistical considerations

A standardised case record form was designed to systematically capture the data pertinent to the study. The data were entered into Microsoft Excel 2016 (Microsoft, Redmond, CA, USA). Data analysis was performed using STATA/SE 11.2 (Stata Corp, College Station, TX, USA). Malnutrition was defined as weight for age < −2 *Z* score or weight for height < −2 *Z* score (for children <5 years) or body mass index for age < −2 *Z* score (for children ≥5 years). We calculated the *Z*-scores using the WHO Anthro software v3.2.2 and Anthro Plus software v1.0.4 for patients below 5 years and above 5 years, respectively. The median follow-up duration was calculated using the reverse Kaplan–Meier method. The Kaplan–Meier method was used to estimate event-free survival (EFS) and OS with corresponding 95% confidence intervals (CIs). An event was defined as treatment abandonment or death due to any cause or relapse or progression of the disease. EFS was calculated from the date of diagnosis to the date of the first documented event. OS was calculated from the date of diagnosis to the date of death due to any cause. The patients without an event or death were censored on the date of the last follow-up. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant.

Results

During the 24-year study period (January 2000 to December 2023), a total of 89 children were evaluated for renal tumours at our centre. Of these, 17 children (19%) were diagnosed with non-Wilms renal tumour. Among the remaining 72 children with a provisional diagnosis of WT, 3 were excluded as they had undergone surgery elsewhere but without a confirmed histopathological diagnosis, complete staging information and essential surgical details. This manuscript reports the clinical characteristics, treatment details and survival outcomes of the remaining 69 children who were diagnosed and managed as WT at our centre during the study period (Figure 1).

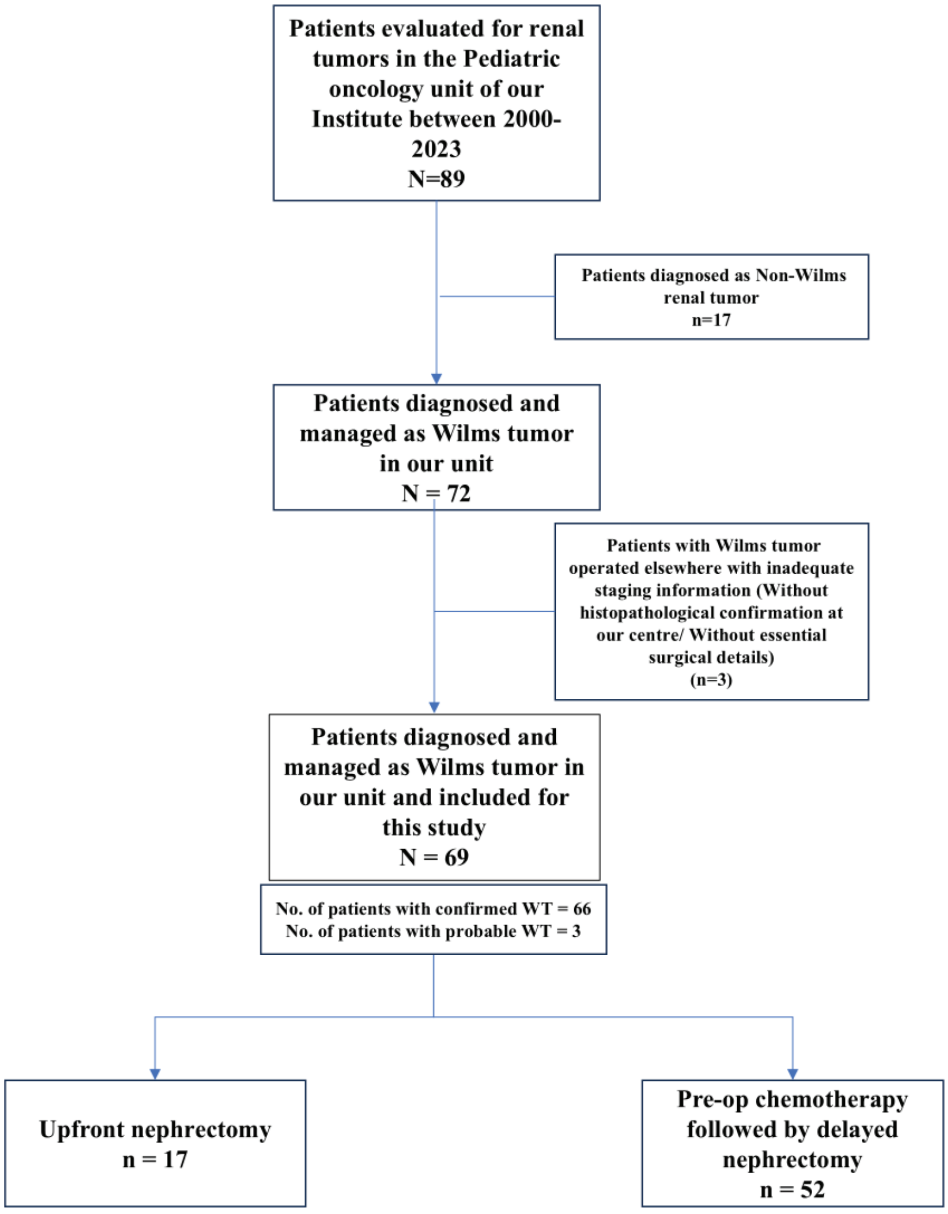


Figure 1. Distribution of children with renal tumour treated in our unit between January 2000 and December 2023.

Baseline characteristics

Among the 69 study subjects, 66 children were classified as confirmed WT while the remaining 3 were categorised as probable WT (Figure 1). The baseline characteristics of the study population are summarised in Table 1. The median age at diagnosis of the study population was 34 months (range: 8–159 months). There was a slight male predominance (M:F ratio 1.22:1) within the study cohort. About 28 out of 69 children (41%) were malnourished at the time of diagnosis. Of the 69 patients, 34 (49%) had right-sided tumours, 32 (46%) had left-sided tumours and the remaining 3 (5%) had bilateral involvement.

Table 1. Baseline characteristics of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69).

Characteristics	Overall (*n* = 69)	Upfront nephrectomy (*n* = 17)	Preoperative chemotherapy followed by delayed nephrectomy (*n* = 52)
Age Median (Range) (mon)	34 (8–159)	33 (8–159)	35 (9–156)
Gender, *n* (%) Male Female	 38 (55%) 31 (45%)	 11 (65%) 6 (35%)	 27 (52%) 25 (48%)
Presenting symptoms, *n* (%) Abdominal mass/distension Abdominal pain Haematuria	 68 (99%) 19 (27%) 12 (17%)	 16 (94%) 4 (23%) 4 (23%)	 52 (100%) 15 (29%) 8 (15%)
Malnutrition, *n* (%)®	28 (41%)	8 (47%)	20 (38%)
Hypertension, *n* (%) Present Absent Not known	 27 (39%) 23 (33%) 19 (28%)	 5 (30%) 4 (23%) 8 (47%)	 22 (42%) 19 (37%) 11 (21%)
Laterality *n* (%) Right Left Bilateral	 34 (50%) 32 (46%) 3 (4%)	 11(65%) 6 (35%) -	 23 (44%) 26 (50%) 3 (6%)
Year of diagnosis 2000–2007 2008–2015 2016–2023	 21 (30%) 26 (38%) 22 (32%)	 6 (35%) 7 (42%) 4 (23%)	 15 (29%) 19 (37%) 18 (34%)

Continued

Table 1. Baseline characteristics of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69). *Continued*

Characteristics	Overall (*n* = 69)	Upfront nephrectomy (*n* = 17)	Preoperative chemotherapy followed by delayed nephrectomy (*n* = 52)
Imaging characteristics Tumour volume (cm^3) Median (Range)*©	360 (87.27–3,000)	318.34 (87.27–1,210.3)	360 (96.25–3,000)
Calcification, *n* (%)@	11 (16%)	3 (18%)	8 (15%)
Intravascular thrombus, *n* (%)#	13 (19%)	2 (12%)	11 (21%)
Lymphadenopathy, *n* (%)$	16 (23%)	6 (35%)	10 (19%)
Metastasis, *n* (%)	16 (23%)		16 (30%)
Lungs	11 (69%)	-	11(69%)
Liver	1 (6%)		1 (6%)
Both lungs and liver	4 (25%)		4 (25%)
Stage distribution[ı]			
Stage I, *n* (%)	23 (33%)		15 (29%)
Stage II, *n* (%)	15 (22%)	8 (47%)	12 (23%)
Stage III, *n* (%)	13 (19%)	3 (18%)	7 (13%)
Stage IV, *n* (%)	14 (20%)	6 (35%)	14 (27%)
Stage V, *n* (%)	3 (4%)		3 (6%)
Unknown stage, *n* (%)	1 (2%)		1 (2%)

*Tumour volume data missing in 8 children; @Calcification data missing in 12 children; #Intravascular thrombus data missing in 15 children; $Lymphadenopathy data missing in 14 children; ®Anthropometric data missing in 4 children; ©Tumour volume = Length (cm) × width (cm) × thickness (cm) × 0.5; ıChildren who underwent upfront nephrectomy were staged according to the NWTS/COG staging system. Children who underwent delayed nephrectomy were staged according to the SIOP staging system

Among the 69 patients in our study cohort, 68 (99%) presented with abdominal mass or distension. In contrast, abdominal pain and haematuria were observed in only 19 (27%) and 12 (17%) patients, respectively. Hypertension at the time of diagnosis was documented in 27 (39%) children. Syndromic features and congenital anomalies were identified in nine children within our study cohort. These included undescended testes in two children, hemihypertrophy in two, horseshoe kidney in two, malrotated kidney in one, renal failure in one and developmental delay in one child. Among the study participants with available imaging details, the median tumour volume was 360 cm^3 (range: 87.27–3,000 cm^3). Calcifications were observed in 11 children (16%), intravascular thrombus in 13 (19%) and regional lymph node metastases in 16 (23%). Metastatic disease at presentation was documented in 16 children, of whom 11 had isolated lung metastases, 1 had isolated liver metastasis and 4 had both lung and liver involvement.

Treatment approach

Eight children who had previously undergone upfront nephrectomy elsewhere and were subsequently treated at our centre were also included in the study, as histopathological diagnosis and staging were confirmed at our institution, and essential surgical details were available. Among the remaining 61 children, 9 children who did not exhibit any of the aforementioned image-defined high-risk features underwent upfront nephrectomy. The remaining 52 children, who had one or more image-defined high-risk features, received preoperative chemotherapy followed by delayed nephrectomy. Although none of the clinical or radiological features showed statistically significant differences between the two treatment groups, children who underwent delayed nephrectomy tended to have larger tumour volumes and a higher incidence of intravascular thrombus, but a lower incidence of regional lymphadenopathy.

Upfront nephrectomy

Among our study cohort, 17 children (8 – elsewhere; 9 – at our centre) underwent upfront radical nephroureterectomy. None of the patients who underwent upfront nephrectomy at our centre had either preoperative or intraoperative tumour spill, whereas four out of eight children (50%) operated upfront elsewhere had tumour spill. One child with an inferior vena cava tumour thrombus (misinterpreted as vessel compression by the mass in the preoperative imaging) who underwent upfront surgery at our institute was found to have gross residual disease postoperatively. The stage distribution among the children who underwent upfront nephrectomy was as follows: Stage I–8 (47%); Stage II–3 (18%) and Stage III–6 (35%). None of the 17 children had unfavourable histology (Table 2). Except for two children who did not receive adjuvant treatment – one due to treatment abandonment and the other due to poor general condition secondary to renal failure – the remaining 15 children received adjuvant chemotherapy: 10 with a two-drug regimen (vincristine and actinomycin D) and 5 with a three-drug regimen (vincristine, actinomycin D and doxorubicin) (Supplementary Figure 1). Additionally, 4 of the 17 children (23%) received flank irradiation.

Table 2. Histologic risk stratification of children with WT treated in our unit from January 2000 to December 2023 (*N* = 69).

Risk	Risk subgroup	*n* (%)
Upfront nephrectomy (*N* = 17)*		
Favourable histology: (*n* = 17)	No anaplasia	17 (100%)
Preoperative chemotherapy followed by delayed nephrectomy (*N* = 52)#		
Low risk: (*n* = 0)	Completely necrotic	-
Intermediate risk: (*n* = 42)	Regressive	8 (15%)
	Mixed	26 (50%)
	Epithelial predominant	2 (4%)
	Stromal predominant	4 (8%)
	Focal anaplasia	2 (4%)
High risk: (*n* = 3)	Blastemal predominant	3 (6%)
	Diffuse anaplasia	-
Unknown (*n* = 7)		7 (13%)

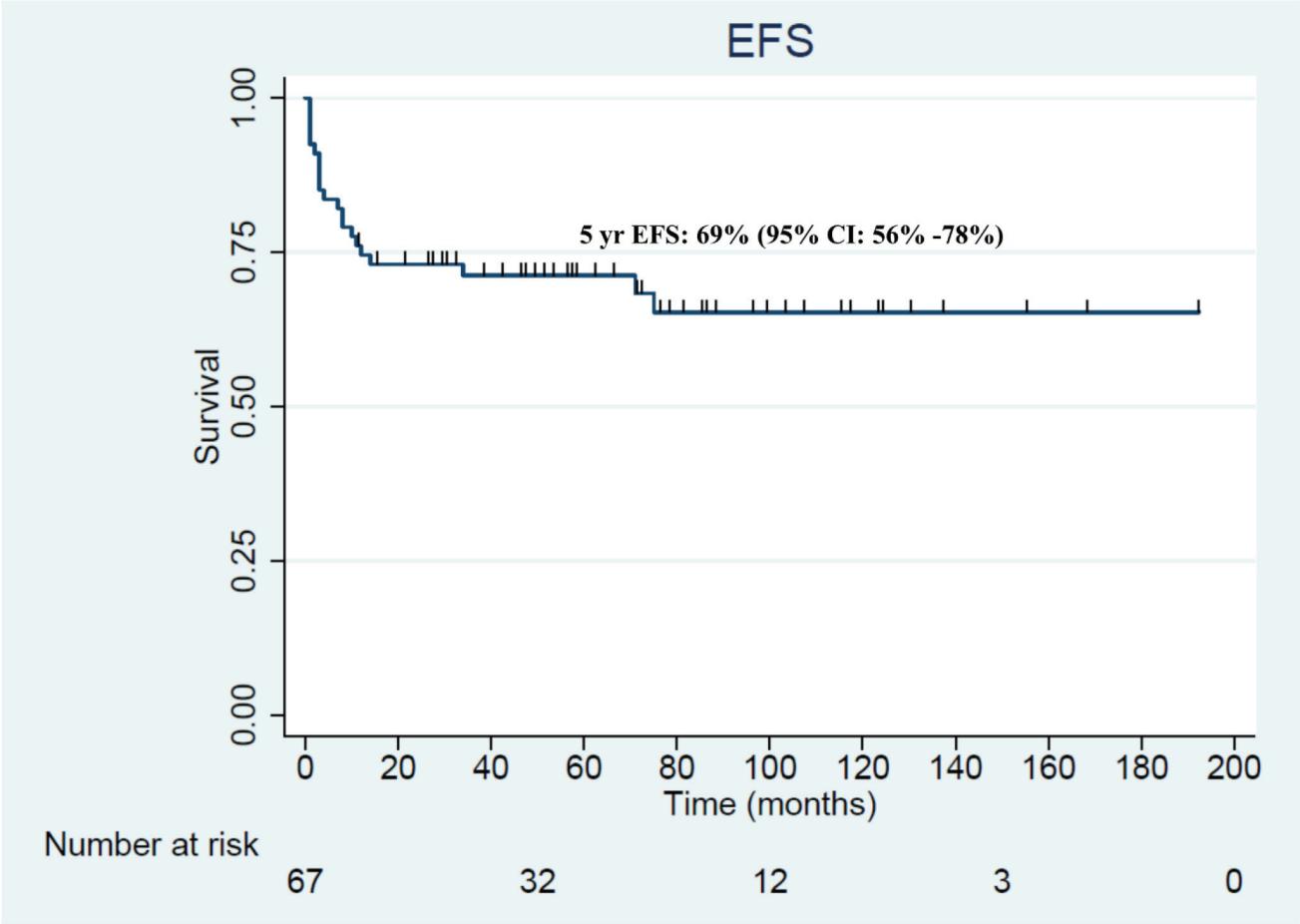
*Children who underwent upfront nephrectomy were risk-stratified according to the NWTS/COG histologic risk-stratification system

#Children who underwent delayed nephrectomy were risk-stratified according to the SIOP histologic risk stratification system

Delayed nephrectomy

Among our study cohort, 52 children received preoperative chemotherapy, including 36 with localised WT and 16 with metastatic disease. Of these, only 25 children (48%) underwent diagnostic biopsy before treatment initiation. Among them, the biopsy findings of 22 children were concordant with the final postnephrectomy histopathological diagnosis. In the remaining three cases, nephrectomy was not performed, precluding histopathological comparison. Of the 36 children with localised disease, 35 received a two-drug preoperative chemotherapy regimen (vincristine and actinomycin D), while 1 child received a three-drug preoperative chemotherapy regimen (vincristine, actinomycin D and doxorubicin/epirubicin). Among the 16 children with metastatic disease, 9 received a two-drug preoperative chemotherapy regimen and the remaining 7 received a three-drug preoperative chemotherapy regimen (Supplementary Figure 2). Postchemotherapy tumour volume measurements were available only for 38 children, of whom 31 (81%) had a residual tumour volume of less than 500 cm^3, including 20 (53%) with a volume of less than 200 cm^3.

Of the 52 children who received preoperative chemotherapy, 6 did not undergo nephrectomy: 3 due to poor general condition secondary to progressive disease; 2 due to treatment abandonment and 1 child with a horseshoe kidney in whom partial nephrectomy was deemed not feasible. Among the remaining 46 children, 2 with bilateral WT and 1 with a horseshoe kidney underwent partial nephrectomy, whereas the remaining 43 underwent radical nephrectomy. Tumour rupture was observed in three children who underwent delayed nephrectomy – two had preoperative rupture and one experienced intraoperative spill.



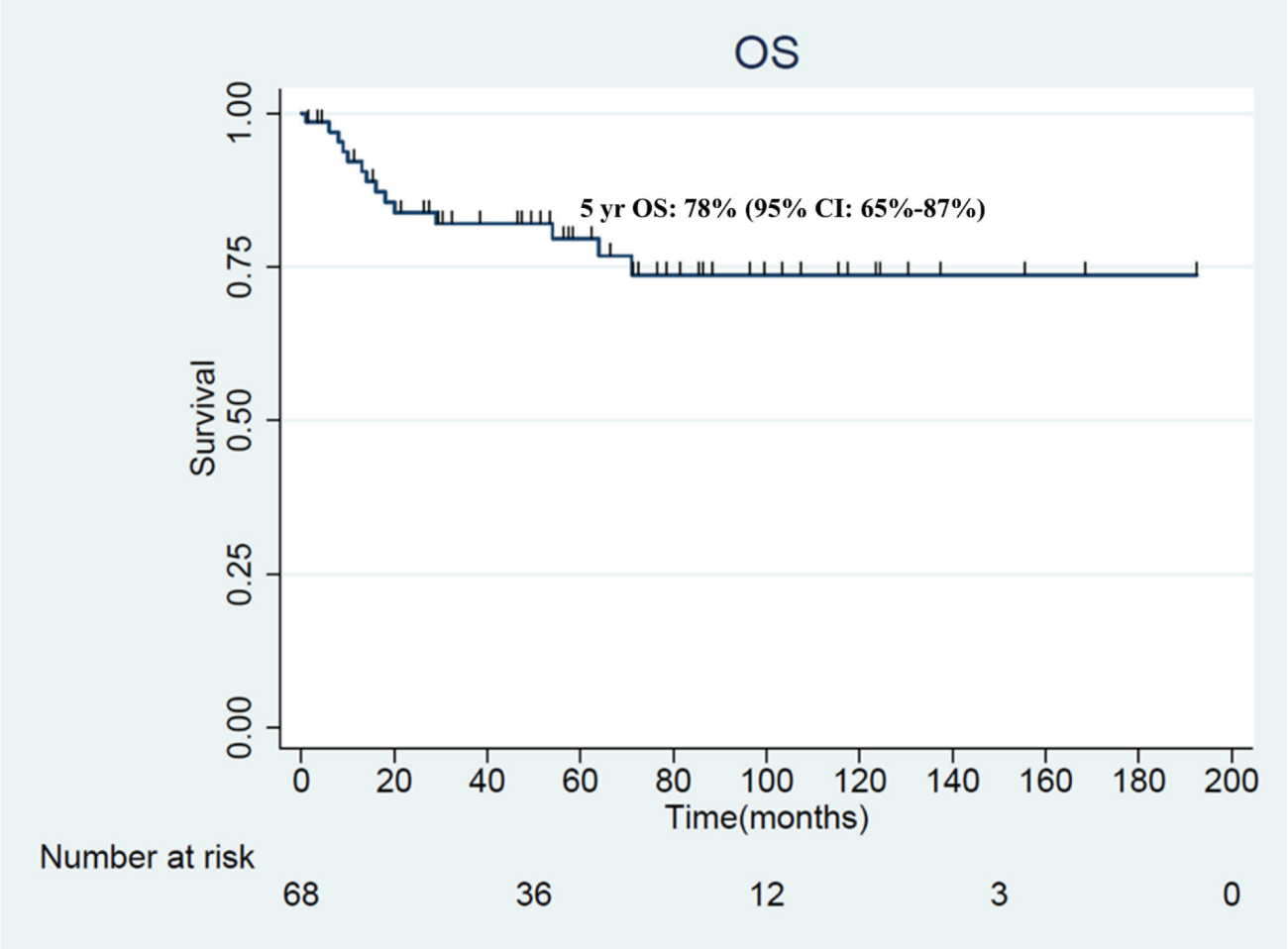


Figure 2. (a): EFS of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69). (b): OS of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69).

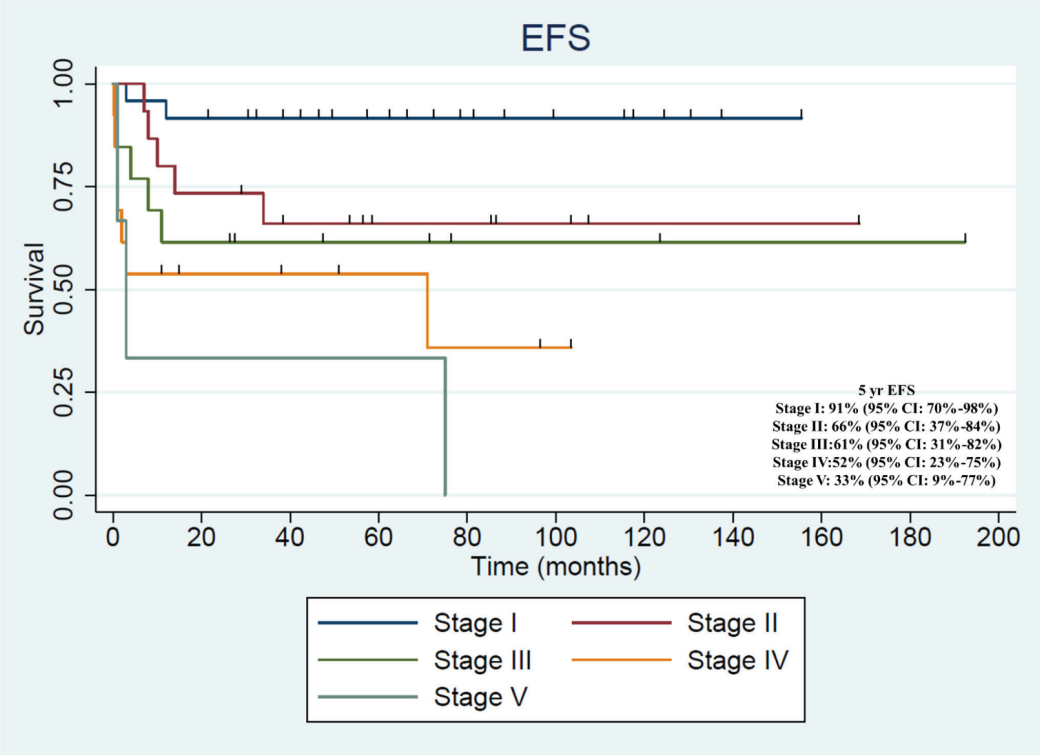
The stage distribution among the 52 children who underwent delayed nephrectomy was as follows: Stage I – 15 (29%); Stage II – 12 (23%); Stage III – 7 (13%); Stage IV – 14 (27%); Stage V – 3 (6%) and Stage not known – 1 (2%). The majority of patients (*n* = 42; 81%) had intermediate-risk histology, with mixed histology being the most common subtype, accounting for half of these cases (Table 2; Supplementary Figures 3 and 4). Among the 46 children who underwent delayed nephrectomy following preoperative chemotherapy, 2 patients abandoned treatment before initiating any adjuvant therapy. Of the 44 children who received adjuvant chemotherapy, 19 received a two-drug regimen (vincristine and actinomycin D), 16 received a three-drug regimen (vincristine, actinomycin D and doxorubicin/epirubicin) and the remaining 9 received a four-drug regimen (cyclophosphamide, doxorubicin, carboplatin and etoposide) (Supplementary Figure 5). Thirteen children (25%) who underwent delayed nephrectomy received radiotherapy: flank alone in nine, whole abdominal irradiation in one, flank plus whole lung irradiation (WLI) in one, WLI alone in one and WLI with liver irradiation in one child.

Survival outcomes

The median follow-up duration of the study participants who remained alive without any evidence of disease was 68.5 months (range: 11–192 months). The 5-year EFS and OS rates of the entire study cohort were 69% (95% CI: 56%–78%) and 78% (95% CI: 65%–87%),

respectively. The Kaplan–Meier survival curves depicting the EFS and OS of the entire study cohort are shown in Figure 2a and b. The 5-year EFS and OS rates for patients with Stage I: 91% (95% CI: 70%–98%) and 91% (95% CI: 70%–98%); Stage II: 66% (95% CI: 37%–84%) and 63% (95% CI: 32%–83%); Stage III: 61% (95% CI: 31%–82%) and 91% (95% CI: 51%–99%); Stage IV: 52% (95% CI: 23%–75%) and 67% (95% CI: 34%–86%); and Stage V: 33% (95% CI: 9%–77%) and 100% (Figure 3a and b). The 5-year EFS and OS rates of the children who underwent upfront nephrectomy were 51% (95% CI: 25%–72%) and 60% (95% CI: 28%–82%), respectively. In comparison, those who underwent delayed nephrectomy had a 5-year EFS of 75% (95% CI: 60%–84%) and OS of 83% (95% CI: 69%–91%). However, these differences were not statistically significant for either the 5-year EFS (p = 0.2) or 5-year OS (p = 0.27) (Figure 4a and 4b). The most common cause of treatment failure among our study cohort was disease relapse (n = 15; 22%), followed by treatment abandonment (n = 8; 11%). Additionally, two children developed second malignant neoplasms: one developed papillary thyroid carcinoma 6 years after treatment completion, and another child developed Ewing sarcoma of the left tibia 2 years after treatment completion.

Among the entire study cohort, univariate analysis showed that the 5-year EFS and OS were significantly influenced by the year of diagnosis and the number of lymph nodes harvested (Supplementary Table 3). The patients diagnosed in more recent years (2016–2023) had significantly superior 5-year EFS and OS (86% and 95%, respectively) compared to those diagnosed in the earlier time periods. Similarly, the patients with at least seven lymph nodes harvested had markedly better 5-year EFS and OS (87% and 92%, respectively) than those with fewer lymph nodes sampled or with missing information (54% and 65%, respectively). Disease stage was significantly associated with 5-year EFS but not OS in the univariate analysis. Multivariate analysis revealed disease stage and treatment approach (upfront nephrectomy versus delayed nephrectomy) as significant independent predictors of both EFS and OS (Supplementary Table 4). Delayed nephrectomy showed lower hazards for events (HR: 0.22; 95% CI: 0.05–0.92); p = 0.04) and mortality (HR: 0.13; 95% CI: 0.02–0.85); p = 0.03). Advanced disease stage is associated with increased risk of poor EFS and OS. Univariate analyses within the upfront and delayed nephrectomy cohorts are separately summarised in Supplementary Tables 5 and 6, respectively. Multivariate Cox regression for both cohorts yielded nonconvergent models due to limited events.



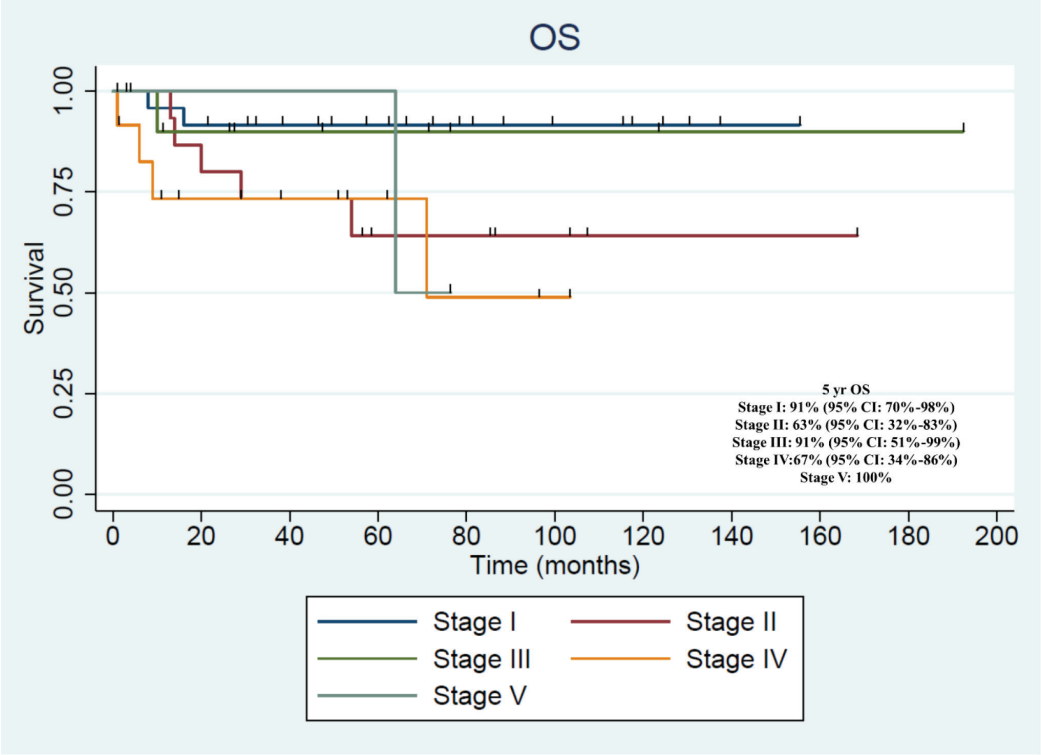


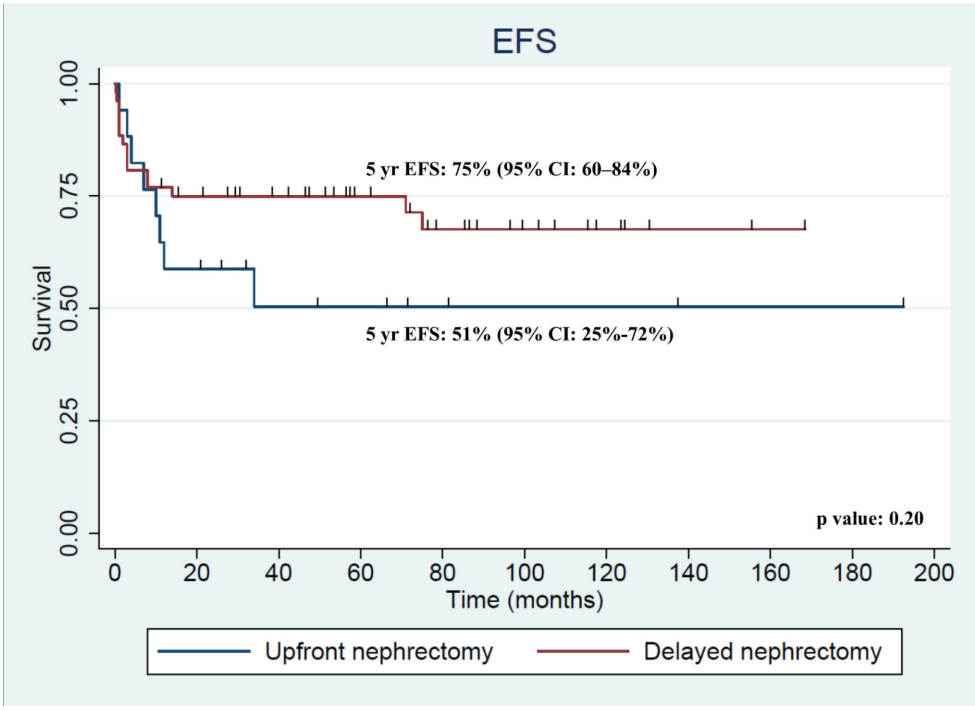
Figure 3. (a): Stage-wise EFS of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69). (b): Stage-wise OS of children with WT treated in our unit between January 2000 and December 2023 (*N* = 69).

Discussion

This study reports the outcomes of children with WTs from a tertiary cancer care centre in an LMIC. With the help of multimodal therapy, we achieved a 5-year EFS of 69% and a 5-year OS of 78%. These findings underscore that, despite intensive multimodal treatment, the outcomes for WT in LMICs remain inferior to those reported in HICs.

WT constituted the majority of renal tumours (81%) in our study cohort. The slight male predominance among our study population contrasts with the global literature. This deviation likely reflects the gender disparity in seeking cancer care in India rather than any underlying biological difference [2, 21]. Among our study cohort, 41% of the children were malnourished at the time of diagnosis. This figure is comparable to the prevalence reported by Rahiman *et al* [22] for children with WT in North India. Among the children with available tumour volume measurements, the median tumour volume at diagnosis in our study population is less than that reported by Rahiman *et al* [22] (481 mL) and Joseph *et al* [23] (559 mL), despite having a similar stage distribution. The prevalence of metastatic disease (23%) and bilateral WT (5%) among our study cohort is consistent with the findings of various Indian and international studies [2, 5].

At our institute, we have adopted a hybrid approach for managing children with renal tumours, exploiting the advantages of both upfront and delayed nephrectomy. Among the patients with WTs in our study cohort, the majority (75%) underwent delayed nephrectomy while the remaining (25%) underwent upfront nephrectomy. In contrast, the Non-Wilms renal tumour cohort from our unit demonstrated a reverse trend, with 65% undergoing upfront nephrectomy and 35% undergoing delayed nephrectomy [24].



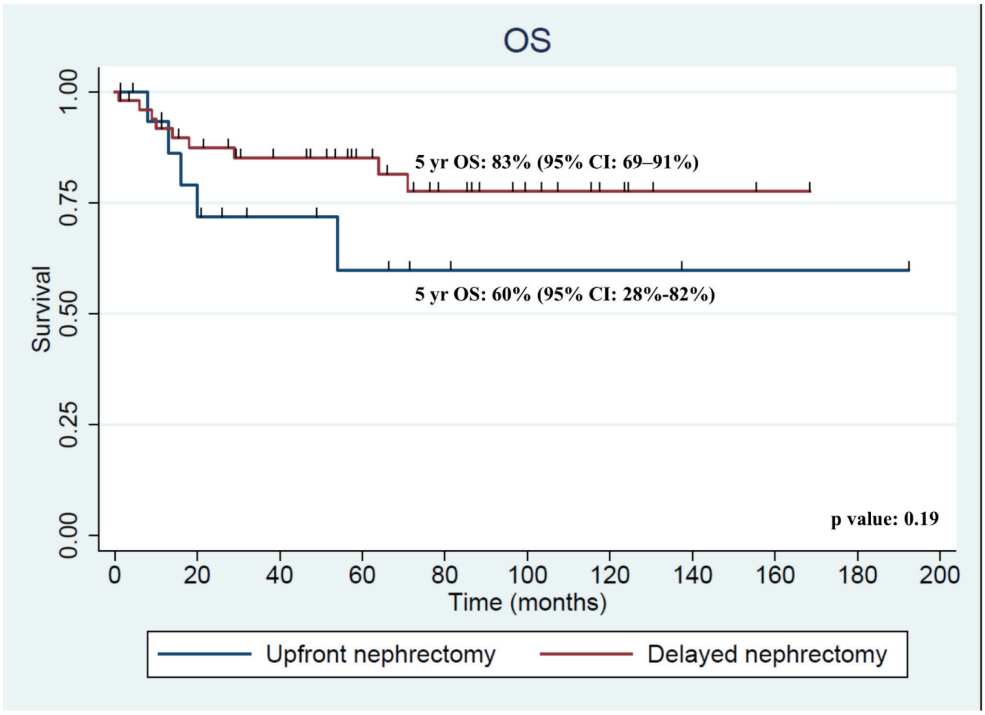


Figure 4. (a): EFS of children with WT who underwent upfront nephrectomy (*n* = 17) versus delayed nephrectomy (*n* = 52) in our unit between January 2000 and December 2023. (b): OS of children with WT who underwent upfront nephrectomy (*n* = 17) versus delayed nephrectomy (*n* = 52) in our unit between January 2000 and December 2023.

Among the nine children who underwent upfront nephrectomy at our institute, none had intraoperative tumour spill, although one child had incomplete resection. Overall, the rate of adverse surgical events among our study cohort who underwent upfront nephrectomy in-house was 3.6%, in stark contrast to 50% among the children who underwent upfront nephrectomy elsewhere (four out of eight had intraoperative tumour spill). This tailored, risk-adapted approach to decide on the timing of surgery based on imaging features has already been prospectively validated by Qureshi *et al* [25] who reported tumour rupture in only 1 of 19 children selected for upfront nephrectomy in the absence of high-risk imaging features. These findings underscore the importance of surgical expertise in WT management and suggest that even in high-volume tertiary centres, restricting upfront nephrectomy only to carefully selected patients at low risk for adverse surgical events would result in a significant reduction in treatment burden.

The 5-year EFS and OS rates of the entire study cohort were 69% (95% CI: 56%–78%) and 78% (95% CI: 65%–87%), respectively. These survival outcomes fall within the range of previously reported survival rates for children with WT in India [5, 6]. Notably, our results lie between the survival outcomes reported for WT in low-income countries and LMICs in Africa and those from HICs [26–28]. This gradient in survival underscores the influence of social determinants of health and the strength of the healthcare system on WT outcomes [5, 29]. Following treatment relapse (22%), treatment abandonment (11%) was the next most common cause of treatment failure. A temporal decline in treatment abandonment was observed, possibly reflecting improved social support systems in more recent years.

While the outcomes of stage I disease were comparable to global standards, the 5-year EFS and OS of stage II disease were notably inferior. Consistent with the findings of Rahiman *et al* [22], we also observed lower survival rates among stage II compared to stage III disease. This paradox may be attributed to inadequate lymph nodal sampling in our study cohort. Only 45% of our study subjects underwent lymph node sampling that met the recommended adequacy criteria – defined as the removal and examination of at least seven lymph nodes – with only 60% of children with stage II disease achieving this benchmark. This suboptimal lymph nodal assessment may have contributed to understaging and, consequently, undertreatment, thereby resulting in inferior outcomes. Notably, inadequate lymph node sampling was documented to be the most common protocol deviation in both resource-replete and resource-limited settings. The adverse impact of inadequate lymph nodal sampling is most pronounced among children with stage II, as documented by Kieran *et al* [30–32]. Furthermore, pathological staging following preoperative chemotherapy requires considerable expertise, as chemotherapy-induced changes within lymph nodes, even in the absence of viable tumour cells, constitute evidence of prior nodal metastasis and warrant classification as stage III under the SIOP staging system [33]. Failure to recognise these treatment-related changes may further contribute to understaging. Supporting this, both lymph node density and log odds of positive lymph nodes, which incorporate not only the number of positive lymph nodes but also the total number of lymph nodes harvested and the number of negative lymph nodes, have recently been identified as important prognostic factors for predicting survival outcomes in children with WT [34–36]. These metrics underscore the importance of meticulous surgical sampling and expert pathological evaluation for accurate staging and appropriate risk-adapted therapy.

Multivariate analysis identified only disease stage and treatment approach (upfront versus delayed nephrectomy) as independent prognostic factors. Compared to upfront nephrectomy, delayed nephrectomy was associated with a significantly lower risk of events and mortality, suggesting that preoperative chemotherapy may confer a survival advantage beyond its traditional role in downstaging and facilitating resection in LMIC settings. While upfront nephrectomy was limited to children with stage I–III disease, delayed nephrectomy was employed across stages I–V. By adjusting for stage as a confounding variable, multivariate analysis effectively unmasked the independent benefit of the delayed nephrectomy approach. Also in our study cohort, increased adverse surgical events associated with upfront nephrectomy performed at peripheral, less-experienced centres negated the benefit of a favourable stage distribution expected out of a tailored, risk-adapted approach to surgical timing.

Our findings emphasise the multifactorial challenges behind poorer WT outcomes in LMICs – socioeconomic constraints, healthcare system gaps and biological factors. Beyond delayed presentation and diagnostic limitations, the limited availability of surgical and pathological expertise hinders accurate staging and risk stratification. Further, additional research into the tumour biology specific to the LMIC context is essential to drive improvements in outcomes. Currently, most studies from LMICs focus predominantly on social and health system factors, with limited data on the biological and molecular characteristics of WT in these settings [29].

Strengths and limitations

This study reports the real-world experience of managing children with WT in a tertiary care centre in Southern India, highlighting the heterogeneity in management. A key strength lies in our adoption of a hybrid approach, wherein the decision between upfront and delayed

nephrectomy was individualised based on multidisciplinary tumour board assessment of clinical and radiological risk factors. Notably, our study is one of the few studies from India that explicitly documents the objective criteria guiding the selection of patients for upfront nephrectomy versus delayed surgery. Our study presents one of the longest single-institution experiences in India, enabling the assessment of trends over time and survival outcomes with an adequate follow-up. By including both upfront and delayed nephrectomy cohorts, this study provides insights into the relative effectiveness and outcomes of each strategy in a real-world resource-limited setting. However, our findings must be interpreted in light of certain limitations. The retrospective study from a single centre is inherently subject to selection bias and missing data. Despite the extended study period, subgroup sizes remained small for certain clinical scenarios, limiting the power of multivariate analyses. Evolving chemotherapy regimens and supportive care practices across two decades may have introduced treatment variability, affecting outcome comparisons. Importantly, our study lacks molecular and biological characterisation of tumours, which is increasingly relevant in contemporary risk stratification. Furthermore, patient-reported outcomes, late toxicities and long-term quality of life were not captured. Nonetheless, our study reinforces the feasibility and potential advantages of a structured, multidisciplinary and individualised approach to WT management in LMICs.

Conclusion

Outcomes for WT in LMICs remain inferior to those reported in HICs, despite multimodal treatment. An individualised, risk-adapted approach to the timing of nephrectomy appears to be a pragmatic strategy in the absence of randomised evidence. Further research addressing both health system barriers and the biological characteristics of WT in LMICs is needed to bridge the survival gap.

List of abbreviations

CECT, Contrast-enhanced computed tomography; CI, Confidence incidence; COG, Children's Oncology Group; CT, Computerised tomography; EFS, Event-free survival; HICs, High-income countries; HR, Hazard ratio; LMICs, Low- and middle-income countries; NWTS, National Wilms Tumor Study Group; OS, Overall survival; PODC, Paediatric Oncology in Developing Countries; SIOP, Société Internationale d'Oncologie Pédiatrique; WHO, World Health Organization; WLI, Whole lung irradiation; WT, Wilms tumour.

Acknowledgment

The manuscript has been read and approved by all the authors. Each author confirms that the manuscript represents honest and original work.

Conflicts of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Funding

The authors received no specific funding for this work.

Financial and non-financial interest declarations

The authors have no relevant financial or non-financial interests to disclose.

Consent to participate

Informed consent was waived off by the Institutional Ethics Committee of Cancer Institute (WIA), with Reg No: ECR/235/Inst/TN/2013/RR-24 (Ref No:IEC/2025/April 25) as this study was a retrospective study using anonymised data.

Consent for publication

Not applicable.

Ethical approval

Human and animal rights: This research involved only human participants.

Ethical approval: Prior approval and clearance were obtained from the Institutional Ethics Committee of Cancer Institute (WIA), with Reg No: ECR/235/Inst/TN/2013/RR-24 (Ref No:IEC/2025/April 25). All procedures performed in our study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Author contributions

VR conceived the concept, overlooked the entire study process and validated the data and manuscript; PS collected the data, performed the formal analysis and prepared the draft of the manuscript; AR verified the data and corrected the manuscript; GD, BTK and GVV corrected the manuscript.

Declaration of artificial intelligence (AI) in scientific writing

The authors declare that no AI tools were used in the preparation of this manuscript.

Clinical trial registration

Not applicable.

Data availability

The data supporting the findings of this study are available with the corresponding author.

Prior presentation

This work was previously presented as a poster at SIOP Asia, Riyadh, Saudi Arabia on April 13–15, 2025.

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Supplementary materials

Supplementary Table 1. NWTS/COG and SIOP staging systems of WT.

Stage	NWTS/COG	SIOP
Stage I	Tumour limited to kidney, completely resected. The renal capsule is intact. The tumour was not ruptured or biopsied prior to removal. The vessels of the renal sinus are not involved. There is no evidence of tumour at or beyond the margins of resection. Notes: by definition, extrarenal tumours cannot be stage I, defined as stage II if completely resected with negative margins or stage III if microscopic or gross residual disease.	Tumour is limited to the kidney. Tumour is present in the perirenal fat but is surrounded by a fibrous (pseudo)capsule. The (pseudo)capsule might be infiltrated by viable tumour, which does not reach the outer surface. Tumour might show protruding (botryoid) growth into the renal pelvis or the ureter but does not infiltrate their walls. The vessels or the soft tissues of the renal sinus are not involved by tumour. Intrarenal vessel involvement might be present.
Stage II	The tumour is completely resected, and there is no evidence of tumour at or beyond the margins of resection. The tumour extends beyond the kidney, as is evidenced by any one of the following criteria: a) there is regional extension of the tumour (i.e. penetration of the renal capsule, or extensive invasion of the soft tissue of the renal sinus); b) blood vessels within the nephrectomy specimen outside the renal parenchyma, including those of the renal sinus, contain tumour.	Viable tumour is present in the perirenal fat and is not covered by (pseudo)capsule, but is completely resected (resection margins are clear). Viable tumour infiltrates the soft tissues of the renal sinus. Viable tumour infiltrates blood and/or lymphatic vessels of the renal sinus or of the perirenal tissue, but it is completely resected. Viable tumour infiltrates the wall of the renal pelvis or of the ureter. Viable tumour infiltrates the vena cava or adjacent organs (except the adrenal gland) but is completely resected.
Stage III	Residual nonhaematogenous tumour present following surgery, and confined to abdomen. Anyone of the following may occur: a) lymph nodes within the abdomen or pelvis are involved by tumour (note: lymph node involvement in the thorax, or other extra-abdominal sites is a criterion for stage IV); b) the tumour has penetrated through the peritoneal surface; c) tumour implants are found on the peritoneal surface; d) gross or microscopic tumour remains postoperatively (e.g., tumour cells are found at the margin of surgical resection on microscopic examination); e) the tumour is not completely resectable because of local infiltration into vital structures; f) tumour spillage occurring either before or during surgery; g) the tumour is treated with preoperative chemotherapy (with or without a biopsy regardless of type – tru-cut, open, or fine needle aspiration) before removal; h) tumour is removed in greater than one piece (e.g. tumour cells are found in a separately excised adrenal gland; a tumour thrombus within the renal vein is removed separately from the nephrectomy specimen). Extension of the primary tumour within the vena cava into the thoracic vena cava and heart is considered stage III, rather than stage IV, even though outside the abdomen.	Viable tumour is present at a resection margin. Nonviable tumour or chemotherapy-induced changes present at a resection margin are not regarded as stage III. Abdominal lymph node involvement is present by either viable or nonviable tumour. Preoperative or intraoperative tumour rupture, if confirmed by microscopic examination (viable tumour at the surface of the specimen at the area of the rupture). Viable or nonviable tumour thrombus is present at resection margins of ureter, renal vein, or inferior vena cava (always discuss resection margins with the surgeon). Viable or nonviable tumour thrombus, which is attached to the inferior vena cava wall, is removed piecemeal by a surgeon. Wedge or open tumour biopsy before preoperative chemotherapy or surgery. Tumour implants (viable or nonviable) are found anywhere in the abdomen. Tumour (viable or nonviable) has penetrated through the peritoneal surface.

Continued

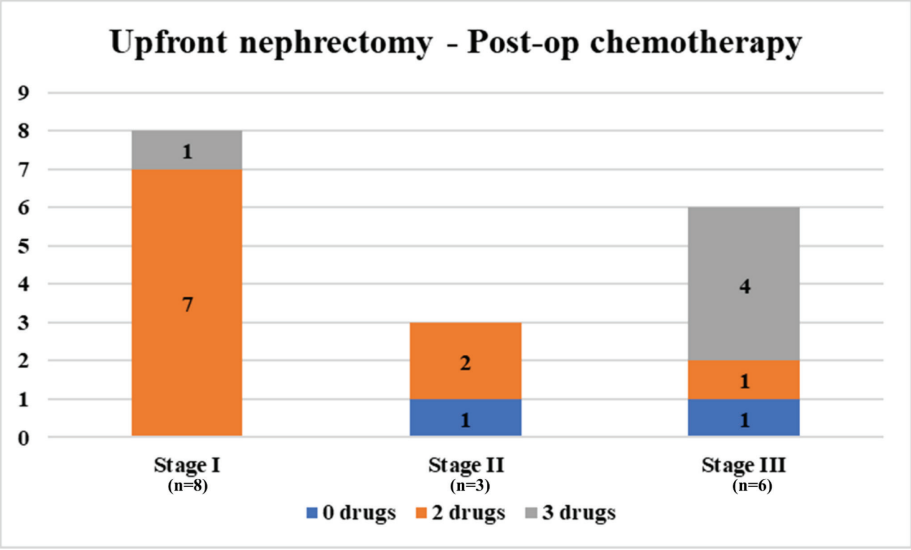
Supplementary Table 1. NWTS/COG and SIOP staging systems of WT. *Continued*

Stage	NWTS/COG	SIOP
Stage IV	Haematogenous metastases (lung, liver, bone, brain, etc.), or lymph node metastases outside the abdominopelvic region are present. (The presence of tumour within the adrenal gland is not interpreted as metastasis and staging depends on all other staging parameters present).	Haematogenous metastases (for example, lung, liver, bone and brain) or lymph node metastases outside the abdominopelvic region.
Stage V	Bilateral tumours at diagnosis; each side should be substaged according to the above criteria	Bilateral renal tumours at diagnosis. Each side should be substaged according to the above criteria.

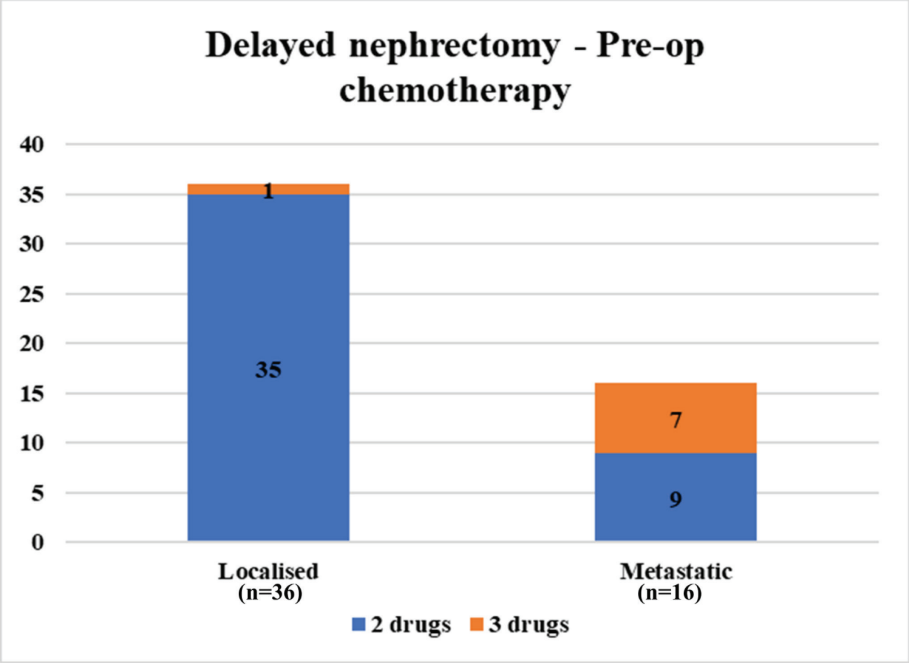
NWTS – National Wilms Tumor Study Group; COG – Children's Oncology Group; SIOP – Société Internationale d'Oncologie Pédiatrique

Supplementary Table 2. NWTS/COG and SIOP histologic risk stratification system of WT.

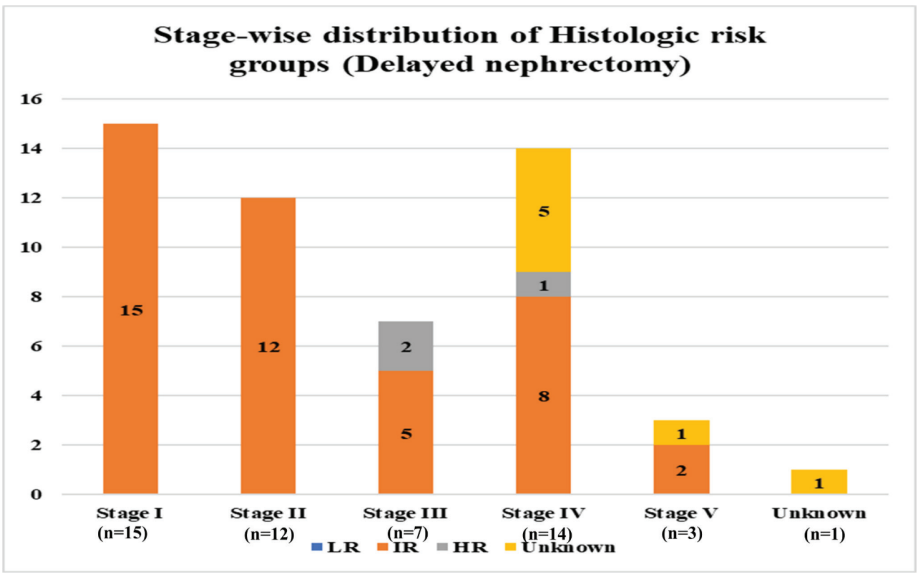
NWTS/COG		SIOP	
Favourable histology	No evidence of any anaplasia	Low risk	Cystic partially differentiated nephroblastoma Completely necrotic nephroblastoma
Unfavourable histology	Focal anaplasia Diffuse anaplasia	Intermediate risk	Nephroblastoma Mixed subtype Regressive subtype Epithelial predominant Stromal predominant Focal anaplasia
		High risk	Blastemal predominant Diffuse anaplasia



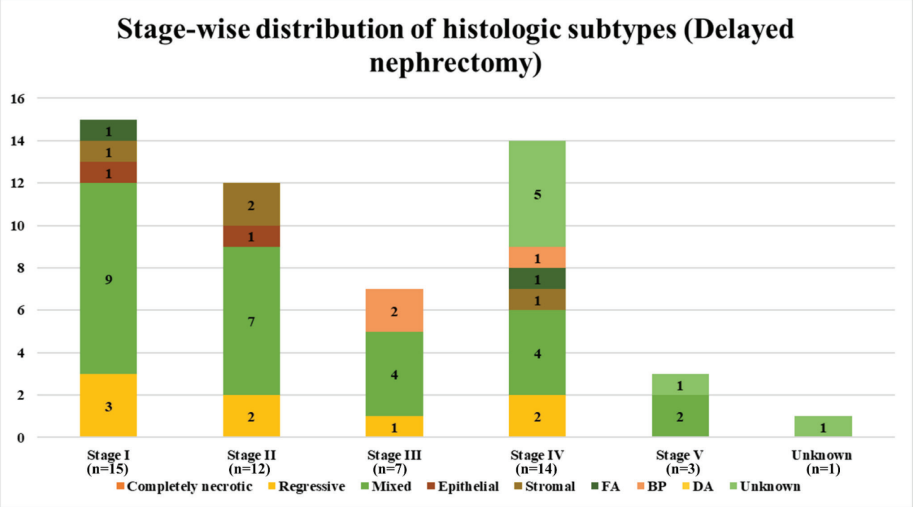
Supplementary Figure 1. Details of postop chemotherapy regimens received by children with WT, who underwent upfront nephrectomy and were treated in our unit between January 2000 and December 2023 (*N* = 17). Staging according to NWTS/COG staging system; 0 drug – No adjuvant postop chemotherapy received; two drugs – received vincristine and actinomycin D; three drugs – received vincristine, actinomycin D and doxorubicin.



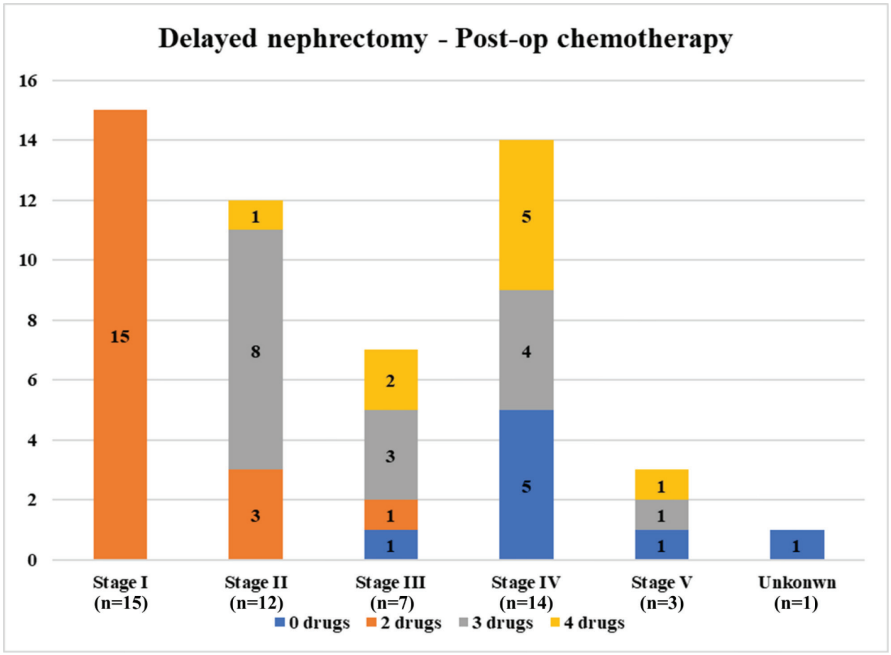
Supplementary Figure 2. Details of preop chemotherapy regimens received by children with WT treated in our unit between January 2000 and December 2023 (*N* = 52). Staging according to the SIOP staging system; two drugs – received vincristine and actinomycin D; three drugs – received vincristine, actinomycin D and doxorubicin/epirubicin.



Supplementary Figure 3. Stage-wise distribution of histologic risk groups among children who underwent delayed nephrectomy in our unit between January 2000 and December 2023 (*N* = 52). Staging according to the SIOP staging system; Risk stratification according to SIOP risk stratification; LR – Low risk; IR – Intermediate risk; HR – High risk.



Supplementary Figure 4. Stage-wise distribution of histologic subtypes among children who underwent delayed nephrectomy in our unit between January 2000 and December 2023 (*N* = 52). Staging according to SIOP staging system; Histologic subtyping according to SIOP histologic classification; FA - Focal anaplasia; BP – Blastemal predominant; DA – Diffuse anaplasia.



Supplementary Figure 5. Details of postop chemotherapy regimens received by children with WT, who underwent delayed nephrectomy and were treated in our unit between January 2000 and December 2023 (*N* = 52). Staging according to the SIOP staging system: 0 drug – No adjuvant postop chemotherapy received; two drugs – received vincristine and actinomycin D; three drugs – received vincristine, actinomycin D and doxorubicin/epirubicin; four drugs - cyclophosphamide, doxorubicin, carboplatin and etoposide.

Supplementary Table 3. Univariate analysis of factors predicting 5-year EFS and OS among children with WT treated in our unit between January 2000 and December 2023 (*N* = 69) using the log-rank test.

		5 years EFS (95% CI)		5 years OS (95% CI)	
Gender	Male	65% (47%–78%)	*p* value: 0.30	76% (58%–87%)	*p* value: 0.56
	Female	74% (55%–86%)		82% (62%–92%)	
Age category	<2 years	62% (36%–80%)	*p* value: 0.22	76% (48%–90%)	*p* value: 0.34
	≥ 2 - < 5 years	79% (62%–89%)		86% (69%–94%)	
	≥ 5 years	46% (16%–72%)		59% (23%–83%)	
Malnutrition	No/Not known	72% (55%–84%)	*p* value: 0.37	77% (58%–88%)	*p* value: 0.78
	Yes	64% (44%–79%)		80% (59%–91%)	
Year of diagnosis	2000–2007	46% (24%–66%)	***p* value: 0.01**	61% (33%–81%)	***p* value: 0.046**
	2008–2015	73% (51%–86%)		76% (54%–88%)	
	2016–2023	86% (62%–95%)		95% (69%–99%)	
Treatment approach	Upfront nephrectomy	51% (25%–72%)	*p* value: 0.20	60% (28%–82%)	*p* value: 0.19
	Delayed nephrectomy	75% (60%–84%)		83% (69%–91%)	
At least seven LN harvested	Yes	87% (69%–95%)	***p* value: 0.0038**	93% (76%–98%)	***p* value: 0.01**
	No/Unknown	54% (37%–68%)		65% (45%–79%)	
Stage	Stage 1	91% (70%–98%)	***p* value: 0.0010**	91% (70%–98%)	*p* value: 0.12
	Stage 2	66% (37%–84%)		63% (32%–83%)	
	Stage 3	61% (31%–82%)		91% (51%–99%)	
	Stage 4	52% (23%–75%)		67% (34%–86%)	
	Stage 5	33% (0%–77%)		100%	

EFS – Event-free survival; OS – Overall survival; LN – Lymph nodes. Bold values: 2 sided *p* value <0.05 - statistically significant

Supplementary Table 4. Multivariate analysis of factors predicting EFS and OS among children with WT treated in our unit between January 2000 and December 2023 (*N* = 69) using a Cox proportional hazards model.

		EFS HR (95% CI)		OS HR (95% CI)	
Gender	Male	1 (Reference)		1 (Reference)	
	Female	0.63 (0.19–2.08)	*p* value: 0.44	1.02 (0.19–5.61)	*p* value: 0.97
Age category	< 2 years	1 (Reference)		1 (Reference)	
	≥ 2 - < 5 years	0.44 (0.13–1.44)	*p* value: 0.17	0.44 (0.09–2.26)	*p* value: 0.33
	≥ 5 years	0.88 (0.21–3.62)	*p* value: 0.86	0.65 (0.09–4.50)	*p* value: 0.67
Malnutrition	No/Not known	1 (Reference)		1 (Reference)	
	Yes	2.68 (0.72–9.98)	*p* value: 0.14	1.28 (0.21–7.80)	*p* value: 0.78
Year of diagnosis	2000–2007	1 (Reference)		1 (Reference)	
	2008–2015	0.47 (0.15–1.44)	*p* value: 0.18	0.32 (0.07–1.38)	*p* value: 0.12
	2016–2023	0.37 (0.08–1.67)	*p* value: 0.20	0.18 (0.02–1.74)	*p* value: 0.13
Treatment approach	Upfront nephrectomy	1 (Reference)		1 (Reference)	
	Delayed nephrectomy	0.22 (0.05–0.92)	***p* value: 0.04**	0.13 (0.02–0.85)	***p* value: 0.03**
Stage	Stage 1	1 (Reference)		1 (Reference)	
	Stage 2	6.21 (0.87–44.56)	***p* value: 0.07**	3.59 (0.48–26.90)	*p* value: 0.21
	Stage 3	3.66 (0.52–25.89)	*p* value: 0.19	0.41 (0.02–7.48)	*p* value: 0.55
	Stage 4	21.06 (2.72–162.78)	***p* value: 0.003**	16.27 (1.65–160.29)	***p* value: 0.017**
	Stage 5	68.39 (6.54–714.68)	***p* value: 0.000**	10.71 (0.42–274.22)	*p* value: 0.15
At least seven LN harvested	Yes	1 (Reference)		1 (Reference)	
	No/Not known	2.67 (0.71–9.94)	*p* value: 0.14	3.53 (0.59–21.12)	*p* value: 0.17

EFS – Event-free survival; OS – Overall survival; LN – Lymph nodes. Bold values: 2 sided *p* value <0.05 - statistically significant

Supplementary Table 5. Univariate analysis of factors predicting 5-year EFS and OS among children with WT who underwent upfront nephrectomy in our unit between January 2000 and December 2023 (*N* = 17) using the log-rank test.

		5 years EFS (95% CI)		5 years OS (95% CI)	
Gender	Male	61% (26%–83%)	*p* value: 0.12	65% (24%–87%)	*p* value: 0.43
	Female	33% (5%–67%)		53% (7%–86%)	
Age category	<2 years	60% (12%–88%)	*p* value: 0.64	60% (13%–88%)	*p* value: 0.91
	≥ 2 - < 5 years	44% (14%–72%)		67% (19%–90%)	
	≥ 5 years	35% (6%–91%)		50% (6%–91%)	
Malnutrition	No/Not known	54% (19%–80%)	*p* value: 0.68	58% (17%–85%)	*p* value: 0.97
	Yes	48% (14%–77%)		67% (18%–91%)	
Year of diagnosis	2000–2007	33% (5%–67%)	*p* value: 0.33	67% (5%–94%)	*p* value: 0.89
	2008–2015	55% (15%–83%)		51% (11%–82%)	
	2016–2023	71% (9%–95%)		71% (9%–95%)	
Surgery done	In house	51% (15%–79%)	*p* value: 0.67	55% (14%–83%)	*p* value: 0.96
	Elsewhere	50% (15%–77%)		69% (21%–91%)	
At least seven LN harvested	Yes	75% (13%–96%)	*p* value: 0.30	75% (13%–96%)	*p* value: 0.61
	No/Not known	44% (17%–69%)		54% (17%–81%)	
Upfront tumour volume >500 cm^3	Yes	37% (13%–96%)	*p* value: 0.95	0%	*p* value: 0.45
	No	53% (24%–76%)		70% (32%–89%)	
Stage	Stage 1	74% (30%–93%)	*p* value: 0.14	74% (30%–93%)	*p* value: 0.05
	Stage 2	0%		0%	
	Stage 3	50% (11%–80%)		100%	
Adjuvant chemotherapy	Two drugs	49% (17%–75%)	*p* value: 0.39	52% (16%–79%)	*p* value: 0.16
	Three drugs	80% (20%–97%)		100%	
Adjuvant radiotherapy	Yes	75% (13%–96%)	*p* value: 0.41	100%	*p* value: 0.18
	No	44% (16%–68%)		49% (16%–76%)	

EFS – Event-free survival; OS – Overall survival; LN – Lymph nodes; Two drugs – Vincristine and actinomycin D; Three drugs – Vincristine, actinomycin D and doxorubicin. Bold values: 2 sided *p* value < 0.05 - statistically significant

Supplementary Table 6. Univariate analysis of factors predicting 5-year EFS and OS among children with WT who underwent delayed nephrectomy in our unit between January 2000 and December 2023 (*N* = 52) using log-rank test.

		5 years EFS (95% CI)		5 years OS (95% CI)	
Gender	Male	66% (45%–81%)	*p* value: 0.07	80% (59%–91%)	*p* value: 0.39
	Female	84% (63%–94%)		87% (65%–96%)	
Age category	<2 years	63% (33%–83%)	***p* value: 0.03**	83% (47%–95%)	*p* value: 0.23
	≥ 2 - < 5 years	90% (71%–96%)		90% (71%–96%)	
	≥ 5 years	43% (12%–71%)		61% (20%–86%)	
Malnutrition	No/Not known	77% (59%–89%)	*p* value: 0.44	83% (63%–92%)	*p* value: 0.74
	Yes	70% (45%–85%)		84% (59%–95%)	
Year of diagnosis	2000–2007	51% (24%–73%)	*p* value: 0.05	60% (28%–81%)	***p* value: 0.01**
	2008–2015	79% (53%–91%)		84% (59%–95%)	
	2016–2023	89% (62%–97%)		100%	
Upfront tumour volume >500 cm^3	Yes	72% (45%–87%)	*p* value: 0.64	82% (54%–94%)	*p* value: 0.95
	No	76% (58%–87%)		84% (66%–93%)	
Postchemo tumour volume <500 cm^3	Yes	83% (65%–93%)	*p* value: 0.06	85% (66%–94%)	*p* value: 0.35
	No	62% (38%–79%)		80% (55%–92%)	
Postchemo tumour volume <200 cm^3	Yes	79% (54%–92%)	*p* value: 0.30	83% (56%–94%)	*p* value: 0.85
	No	72% (53%–84%)		84% (65%–93%)	
At least seven LN harvested	Yes	89% (69%–96%)	***p* value: 0.01**	96% (76%–99%)	***p* value: 0.02**
	No/Unknown	59% (37%–75%)		69% (45%–84%)	
Preop chemotherapy	Two drugs	75% (59%–85%)	*p* value: 0.49	85% (70%–93%)	*p* value: 0.94
	Three drugs	73% (29%–92%)		73% (29%–93%)	
Stage	Stage 1	100%	***p* value: 0.0002**	100%	*p* value: 0.07
	Stage 2	83% (48%–96%)		83% (47%–95%)	
	Stage 3	71% (26%–92%)		85% (30%–98%)	
	Stage 4	62% (23%–75%)		67% (34%–86%)	
	Stage 5	33% (9%–77%)		100%	
Histology	IR	83% (68%–92%)	*p* value: 0.42	90% (75%–96%)	*p* value: 0.56
	HR	100%		100%	
Adjuvant chemotherapy	Two drugs	95% (68%–99%)	*p* value: 0.12	95% (67%–99%)	*p* value: 0.10
	Three drugs	75% (46%–90%)		80% (51%–93%)	
	>3 drugs	100%		100%	
Adjuvant radiotherapy	Yes	85% (51%–96%)	*p* value: 0.52	92% (57%–99%)	*p* value: 0.27
	No	71% (54%–83%)		80% (63%–90%)	

EFS – Event-free survival; OS – Overall survival; LN – Lymph nodes; IR – Intermediate risk; HR – High risk; Two drugs – Vincristine and actinomycin D; Three drugs –Vincristine, actinomycin D and doxorubicin/epirubicin; > 3 drugs – cyclophosphamide, doxorubicin, carboplatin and etoposide. Bold values: 2 sided *p* value < 0.05 - statistically significant