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Prognostic Determinants of Survival, Relapse, and Chemoresistance in Unilateral Wilms Tumor: A 10-Year Real-World Cohort Study from the Caucasus Region

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Abstract

Background

Although survival outcomes for unilateral Wilms tumor (WT) are generally favorable, clinically meaningful heterogeneity persists across risk groups, and real-world evidence on the prognostic value of treatment-response dynamics remains limited. Comprehensive cohort data from the Caucasus–Central Asia region are also scarce. We aimed to evaluate survival outcomes and identify prognostic determinants in a 10-year single-center SIOP-treated cohort from this underrepresented setting.

Methods

We retrospectively analyzed 59 consecutive pediatric patients with unilateral WT treated according to SIOP protocols between 2010 and 2020. Response to pre-operative chemotherapy was assessed by standardized abdominal ultrasonography criteria. Overall survival (OS) and disease-free survival (DFS; time from diagnosis to relapse or death, whichever occurred first) were estimated using Kaplan–Meier methods, and prognostic factors were evaluated using Cox proportional hazards regression.

Results

The median age at diagnosis was 4.3 years, and most patients presented with Stage II–III disease. Pre-operative chemotherapy resulted in regression in 84.7% of cases, stable disease in 8.5%, and progression (chemoresistance) in 6.8%. Median follow-up was 89 months. One-, three-, and five-year OS rates were 96%, 92%, and approximately 88–90%, respectively, and median OS was not reached. Relapse events clustered early, with ~ 80% occurring within the first 24 months; median DFS was 19–21 months. In Cox analyses, Stage III–IV disease and chemoresistance were strongly associated with inferior OS and DFS ($p < 0.05$). Thrombocytopenia was also associated with worse OS and DFS, while neutropenia was associated with relapse risk.

Conclusions

This study provides one of the first large real-world unilateral WT datasets from the Caucasus–Central Asia region and offers implementation-focused evidence relevant to other resource-constrained settings. We confirm an early relapse window (≤ 24 months) and highlight the prognostic relevance of ultrasound-defined progression during pre-operative therapy (chemoresistance) within a standardized SIOP framework. Associations between hematologic toxicity markers and outcomes suggest that routinely available clinical parameters may complement conventional risk factors and help refine risk assessment and follow-up prioritization.

1 | Introduction

Wilms tumor (nephroblastoma) is the most common malignant kidney tumor in childhood and accounts for the majority of pediatric kidney cancers [1]. Current SIOP and COG protocols have achieved five-year

overall survival (OS) rates of over 90% in high-income countries (this rate is confirmed by recent data showing clinically significant heterogeneity persists, with a five-year OS of 93.6% in a 2024 SEER database analysis [2]), current prognostic factors (stage, histology, and 1p/16q LOH) explain only about one-third of relapse cases. Current prognostic factors (stage, histology, and 1p/16q LOH) account for only about one-third of relapse cases, necessitating the integration of biological markers and precision medicine approaches to better predict disease course [3,9]. Despite intensification strategies, outcomes in high-risk and recurrent Wilms tumors remain suboptimal, particularly in unfavorable histologic subtypes. This underscores the need for reliable early risk signals beyond basic staging [4–6]. Large datasets and nomograms highlight the prognostic value of stage and clinicopathological variables, but surgical quality, particularly adequate lymph node sampling, remains important for local control and survival [7,8]. Recent reviews have identified Wilms tumor as a disease with high survival rates but clinically meaningful heterogeneity. Recent reviews characterize Wilms tumor as a disease with high survival rates but clinically meaningful heterogeneity, supporting risk-adapted strategies reinforced by accessible markers given treatment toxicities and late effects [12].

Considering regional resource limitations, pre-operative response assessment at our center is primarily performed using abdominal ultrasonography in accordance with SIOP protocols, reflecting real-world practice in many pediatric oncology centers across Europe and Asia.

Within this context, the aim of the present study was to evaluate a 10-year clinical experience in children diagnosed with unilateral Wilms tumor, to determine overall and relapse-free survival outcomes, and to investigate the association of prognostic factors including stage, histologic risk group, response to chemotherapy, hematologic toxicity, and surgical characteristics with survival and relapse risk.

Novelty and global relevance: This study is designed not as a region-specific report, but as an application-focused contribution within the standardized SIOP framework. We highlight three transferable signals relevant to many settings with limited resources: (i) a dense early relapse period (≤24 months) consistent with the concept of conditional survival, after which risk decreases significantly and provides a pragmatic framework for surveillance prioritization. (ii) Ultrasound-defined progression (chemoresistance) as a feasible, radiation-sparing high-risk marker; this clinical signal serves as a vital substitute for aggressive biological factors such as 1q loss or ALPK2/PRKDC mutations in settings where molecular profiling is inaccessible. (iii) The prognostic contribution of routinely obtainable hematologic markers, particularly thrombocytopenia, as a “clinically actionable” biomarker reflecting tumor aggressiveness and blastemal burden. Real-world datasets from the Caucasus region are insufficient; our cohort closes the survival gap by achieving results (88-90% OS) similar to the 2024 SEER database reference values (93.6%), demonstrating that systematic SIOP compliance can globally equalize care standards.

2 | Materials and Methods

2.1 Study design and setting . . This retrospective, single-center cohort study was conducted at the Department of Pediatric Oncology, National Center of Oncology, Baku, Azerbaijan. The study included all consecutive patients with unilateral Wilms tumor treated according to SIOP protocols between January 1, 2010, and December 31, 2020. A total of 59 consecutive pediatric patients met the eligibility criteria. We followed the STROBE guidelines to ensure the robustness of this retrospective analysis and reduce selection bias. Data completeness was exceptionally high, with missing values for primary outcomes below 5%, ensuring the reliability of the Cox proportional hazards model in this longitudinal cohort.

To minimize selection bias, all consecutive eligible patients were included without exclusions. To reduce information bias, data were collected using a standardized data collection form, and key variables were cross-checked against medical records and pathology reports.

***2.2 Patients and eligibility criteria/*ş** Inclusion criteria were age 0–18 years at initial diagnosis, histologically confirmed unilateral Wilms tumor, and disease stage I–IV according to the SIOP classification. Completion of treatment and availability of essential clinical and pathological data were required.

Exclusion criteria included bilateral (stage V) Wilms tumor, presentation with relapse (patients previously treated at another institution and referred with recurrent disease), incomplete histopathologic data, follow-up duration shorter than 6 months, treatment not compliant with SIOP protocols, and partial treatment performed outside the country.

2.3 Diagnostic work-up and staging. . Initial evaluation included clinical examination, laboratory investigations, abdominal ultrasonography (US), and contrast-enhanced computed tomography (CT) performed solely for diagnostic purposes. To minimize radiation exposure, CT imaging was acquired with a slice thickness of 3–5 mm and was used only at diagnosis. Magnetic resonance imaging (MRI) was not performed.

All imaging during treatment response assessment and follow-up was conducted exclusively using abdominal ultrasonography. US measurements were performed in standardized projections by the same pediatric radiologist or a trained specialist.

Pulmonary metastases were evaluated using chest CT and/or chest radiography.

Tumor staging (stage I–IV) and histologic risk group were determined based on surgical specimens according to SIOP criteria. Pathologic evaluation included assessment of blastemal components, degree of necrosis, and histologic subtype.

***2.4 Treatment protocol*/** . All patients received neoadjuvant (pre-operative) chemotherapy in accordance with SIOP principles, followed by radical nephrectomy with regional lymph node sampling when indicated. Post-operative chemotherapy was administered based on final stage and histologic risk group. Radiotherapy was reserved for cases with locally advanced disease, residual tumor tissue, or metastatic involvement.

According to treatment response data, most patients demonstrated tumor regression or stable disease following pre-operative therapy, while a subset exhibited disease progression (chemoresistance).

Response to chemotherapy was assessed by measuring the largest axial tumor diameter on ultrasonography. Response categories were defined as follows:

- **Complete regression:** complete disappearance of measurable tumor tissue
- **Partial regression:** ≥30% reduction in tumor size
- **Stable disease:** <30% reduction and <20% increase
- **Progression:** ≥20% increase in tumor size and/or appearance of new lesions

Pre-operative progression was defined as chemoresistance.

2.5 Data collection and variables

Data were extracted from electronic and written hospital medical records using a standardized data collection form. The following variables were recorded:

- **Demographic variables:** age group, sex
- **Tumor characteristics:** laterality (right/left), stage, histologic subtype, risk group, blastemal component, presence of metastasis
- **Treatment-related variables:** neoadjuvant and adjuvant chemotherapy, surgical details, radiotherapy, radiologic treatment response
- **Hematologic toxicity:** thrombocytopenia and neutropenia graded according to CTCAE version 5.0
- **Outcomes:** date of diagnosis, date of last follow-up, relapse, death, cause of death

The timing and pattern of relapse (local, pulmonary, or combined) were analyzed separately.

Data completeness was high, with missing data rates below 5% for key clinical and pathological variables. As missing values were considered random, no imputation was performed, and all analyses were conducted using a complete case approach.

2.6 Endpoints and definitions

The primary endpoints were overall survival (OS) and disease-free survival (DFS).

- **Overall survival (OS):** time from diagnosis to death from any cause or last follow-up
- **Disease-free survival (DFS):** time from diagnosis to relapse, death, or last follow-up

For DFS analyses, an event was defined as the first occurrence of relapse or death, whichever occurred earlier

Relapse was defined as radiologically and/or histologically confirmed tumor recurrence. An early relapse window of 24 months was analyzed separately.

The median follow-up duration was calculated using the reverse Kaplan–Meier method to account for censored observations.

2.7 Ethical considerations

This study was approved by the Ethics Committee of the National Center of Oncology (Ethics Protocol No.: MOM-2025/47; approval date: October 7, 2024).

The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective study design, all data were anonymized, and written informed consent was waived.

2.8 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as median and interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. Comparisons between groups were conducted using the chi-square test or Fisher's exact test, as appropriate.

Overall survival (OS) and disease-free survival (DFS) were estimated using the Kaplan–Meier method, and survival curves were compared using the log-rank test. OS was defined as the time from diagnosis to death from any cause or last follow-up, and DFS as the time from diagnosis to relapse, death, or last follow-up.

The median follow-up duration was calculated using the reverse Kaplan–Meier method to account for censored observations.

Univariable and multivariable Cox proportional hazards regression analyses were performed to identify prognostic factors associated with OS and DFS. Variables included in the Cox models were selected based on clinical relevance and prior evidence and included disease stage, histologic risk group, response to pre-operative chemotherapy (regression, stable disease, progression/chemoresistance), hematologic toxicity (thrombocytopenia and neutropenia), and selected treatment-related variables. Results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

The proportional hazards assumption was assessed graphically and was considered acceptable for the final models. A two-sided p value < 0.05 was considered statistically significant. Variables showing a trend toward significance were reported accordingly.

3 | Results

Between 2010 and 2020, 59 pediatric patients with unilateral Wilms tumor treated according to SIOP protocols were included in this retrospective cohort. Baseline demographic, clinical, and pathological

characteristics are summarized in Table 1. The median age at diagnosis was 4.3 years (use either correct IQR here OR change to range), and 55.9% of patients were male. Tumors were left-sided in 55.9% and right-sided in 44.1% of cases. Most patients presented with Stage II (39.0%) or Stage III (32.2%) disease, while 23.7% had Stage IV disease. Blastemal-predominant and mixed histologic subtypes were the most common, each accounting for 28.8% of cases.

Table 1
Baseline Demographic. Clinical. and Pathological Characteristics

Variable	Category	n (%)
Age at diagnosis	Median (range)	4.3 years (3 months–6 years)
Sex	Male	33 (55.9%)
	Female	26 (44.1%)
Tumor laterality	Left	33 (55.9%)
	Right	26 (44.1%)
Stage (SIOP)	Stage II	23 (39.0%)
	Stage III	19 (32.2%)
	Stage IV	14 (23.7%)
Risk group (SIOP)	Low	3 (5.1%)
	Intermediate	33 (55.9%)
	High	23 (39.0%)
Histology	Blastemal predominant	17 (28.8%)
	Mixed type	17 (28.8%)
	Others*	25 (42.4%)
Pre-operative chemotherapy	SIOP protocol (2001–2016)	59 (100%)
Chemotherapy response	Regression	50 (84.7%)
	Stable disease	5 (8.5%)
	Progression (chemoresistance)	4 (6.8%)
Radiotherapy	Yes	**28 (47.5%)**
Follow-up duration	Median	89 months
Footnotes:		
Others include epithelial and stromal predominant histologies.		
No patients were classified as Stage I.		

Baseline characteristics of 59 pediatric patients with unilateral Wilms tumor treated according to SIOP protocols (2010–2020), including age at diagnosis, sex, tumor laterality, SIOP stage, SIOP risk group, histology, pre-operative chemotherapy protocol, ultrasonography-defined chemotherapy response, use of

radiotherapy, and follow-up duration. *Others include epithelial and stromal predominant histologies; no patients were classified as Stage I.*

Response to pre-operative chemotherapy was assessed using abdominal ultrasonography. All patients received SIOP pre-operative chemotherapy, and response categories (Table 4) were tumor regression in 84.7%, stable disease in 8.5%, and progression (chemoresistance) in 6.8% of patients. The median follow-up duration was 89 months.

Overall survival (OS) is shown in Fig. 1A. Seven deaths (11.9%) occurred, and median OS was not reached. The 1-, 3-, and 5-year OS rates were 96%, 92%, and approximately 88–90%, respectively. The most pronounced decline in OS occurred at 26 months, corresponding to three deaths within the same period.

Disease-free survival (DFS) is shown in Fig. 1B and demonstrated greater variability. A total of 11 relapses (18.6%) were observed, with a median DFS of 19–21 months; approximately 80% of relapses occurred within the first 24 months. Relapse was primarily detected by ultrasonography, with computed tomography performed when clinically indicated. Notably, relapse peaks occurred at 19 and 21 months, supporting the concept of an early relapse window in this cohort.

Disease stage remained the strongest classical prognostic factor. Patients with Stage III–IV disease had significantly inferior OS and DFS compared with those with Stage II disease (OS: p = 0.004; DFS: p = 0.002), as illustrated in Table 3 and Table 2, respectively, and supported by Cox regression analyses.

Table 2
Factors Associated With Disease-Free Survival (DFS) — Cox Regression

Variable	HR	95% CI	p
Stage IV vs II-III	16.07	1.97–131.15	**0.010**
High SIOP risk	4.89	1.30–18.48	**0.019**
Chemotherapy progression (chemoresistance)	10.42	0.03–0.51	**0.004**
Thrombocytopenia	8.076	2.33–27.97	**0.001**
Neutropenia	10.619	1.33–85.01	**0.026**

Univariable Cox proportional hazards regression results for DFS, reporting hazard ratios (HRs), 95% confidence intervals (CIs), and p-values for disease stage, SIOP risk group, chemotherapy progression (chemoresistance), thrombocytopenia, and neutropenia.

Table 3
Factors Associated With Overall Survival (OS) — Cox Regression

Variable	HR	95% CI	p
Thrombocytopenia	9.288	2.07–41.76	**0.004**
Chemotherapy progression (chemoresistance)	13.406	1.88–95.38	**0.010**
Neutropenia	6.109	0.71–52.30	0.099 *(trend)*

Univariable Cox proportional hazards regression results for OS, reporting hazard ratios (HRs), 95% confidence intervals (CIs), and p-values for thrombocytopenia, chemotherapy progression (chemoresistance), and neutropenia.

Tablo 4. Response to SIOP Pre-operative Chemotherapy and Associated Outcomes

Response category	Definition	Relapse (%)	Deaths (%)	DFS (Cox)	OS (Cox)
Regression	≥ 30% reduction in tumor size	10% (5/50)	4% (2/50)	Reference	Reference
Stable disease	No significant change	20% (1/5)	0% (0/5)		
Progression (chemoresistance)	Increase in tumor size	75% (3/4)	50% (2/4)	**p = 0.001**	**p = 0.001**

Association between ultrasonography-defined response after SIOP pre-operative chemotherapy (regression, stable disease, and progression/chemoresistance) and clinical outcomes, including relapse and death rates; Cox model comparisons are presented with regression as the reference category.

Table 5. Hematologic Toxicity as Prognostic Factors — Cox Regression

Variable	Endpoint	HR	95% CI	p
Thrombocytopenia	DFS	8.08	2.33–27.97	**0.001**
Thrombocytopenia	OS	7.07	1.25–39.87	**0.027**
Neutropenia	DFS	10.62	1.33–85.01	**0.026**
Neutropenia	OS	6.11	0.71–52.30	0.099 *(trend)*

Cox regression analysis assessing thrombocytopenia and neutropenia as prognostic factors for DFS and OS, reporting hazard ratios (HRs), 95% confidence intervals (CIs), and p-values for each endpoint.

A key finding was the prognostic impact of response to SIOP pre-operative chemotherapy. Among patients with progression during therapy (chemoresistance; n = 4), three experienced relapse (75%) and two died (50%). Chemoresistance was strongly associated with inferior OS and DFS (p = 0.001) (Table 4

and Fig. 1A–1B), underscoring the clinical relevance of dynamic treatment response within a standardized SIOP framework and aligning with ongoing efforts toward response-based risk stratification.

Hematologic toxicity parameters also demonstrated prognostic value. Thrombocytopenia was associated with inferior OS (p = 0.018) and DFS (p = 0.009), while neutropenia was associated with relapse risk (p = 0.007) and showed a non-significant trend toward worse OS (p = 0.068) (Table 5).

Overall, survival outcomes in unilateral Wilms tumor were comparable to contemporary SIOP-reported results. The concentrated early relapse period, the adverse association of chemoresistance, and the contribution of readily available clinical parameters such as hematologic toxicity support the potential value of incorporating time-dependent response signals into pragmatic risk assessment and follow-up prioritization.

4 | Discussion

In comparison with international Wilms tumor literature, our findings extend real-world evidence from an underrepresented setting and provide practice-informing signals that are transferable to other centers implementing SIOP care in resource-constrained environments. In our cohort, the 1-, 3-, and 5-year overall survival (OS) rates of 96%, 92%, and 88–90%, respectively, are largely consistent with contemporary international series and comparable to leading cohorts [13–15]. Our 5-year OS rate of 88–90% is quite comparable to the 5-year survival rate of 93.6% reported in the 2024 SEER database analysis of 2,273 patients. This comparison confirms that the systematic application of SIOP protocols in the Caucasus region can yield results approaching the survival dynamics observed in high-income countries (90%+), despite regional resource limitations.

Analysis of relapse dynamics showed that approximately 80% of events occurred within the first 24 months, with a median disease-free survival (DFS) of 19–21 months. The identification of relapse peaks at 19 and 21 months provides the first regional confirmation of the SIOP “early relapse window” concept and supports a pragmatic surveillance-prioritization approach emphasizing the first two years after diagnosis. While prior studies have primarily linked relapse risk to stage, tumor size, and histologic features, the temporal clustering of relapse has rarely been characterized with similar precision [16–18]. Our findings indicate that surveillance strategies in the Caucasus population should focus particularly on the first two years after diagnosis, after which relapse risk declines substantially.

Our finding that ultrasound-defined progression (chemotherapy resistance) is a strong predictor of poor survival (p = 0.001) is consistent with 2024 exome sequencing data. Somatic variants in genes such as ALPK2, C16orf96, PRKDC, and SVIL have been identified as new drivers of chemotherapy resistance in advanced-stage WT. Although our study relies on ultrasound monitoring that spares radiation, these clinical signals likely reflect underlying aggressive molecular alterations and offer a feasible “clinically actionable” alternative for molecular resistance in settings where advanced sequencing is not feasible [19–20].

These findings support the concept that response-based stratification within the SIOP framework has tangible prognostic value in real-world practice and should be formally considered in future risk models.

To date, biomarker research in Wilms tumor has largely focused on molecular alterations and tissue-based scoring systems [21–23]. In contrast, our study identifies hematologic toxicity, particularly thrombocytopenia and neutropenia, as clinically meaningful and readily measurable prognostic indicators. Thrombocytopenia was significantly associated with lower OS ($p = 0.018$) and DFS ($p = 0.009$), while neutropenia showed a significant association with the risk of relapse ($p = 0.007$). These findings suggest that hematologic changes may reflect the underlying tumor's aggressiveness and treatment resistance rather than being isolated adverse effects. While most series report hematologic toxicity primarily as a safety outcome, our results demonstrate a more systematic relationship with survival and relapse [24–27]. Additionally, research emerging in 2025 highlights that host hematologic responses may serve as therapeutic biomarkers and potentially reflect higher blastemal burden and innate resistance to cytotoxic regimens. Integrating these low-cost markers into risk stratification models could improve the prioritization of follow-up in resource-limited settings.

From a clinical perspective, these findings suggest that Wilms tumor risk models could potentially be expanded beyond stage and histology to incorporate hematologic toxicity profiles observed during treatment. Patients exhibiting unexpectedly severe or prolonged thrombocytopenia or neutropenia may represent a subgroup with higher blastemal burden and resistance to cytotoxic regimens, warranting earlier consideration of intensified or alternative therapeutic strategies [28–30]. Consequently, hematologic toxicity parameters may function as low-cost, widely accessible, real-time “clinic-ready” biomarkers within risk stratification frameworks.

Ultrasound-based response assessment represents a methodological advantage, particularly in pediatric populations, as it minimizes radiation exposure and provides a feasible monitoring approach for resource-limited centers. Overall, our findings suggest that baseline risk factors alone may be insufficient to capture prognosis in real-world practice, and that time-dependent response signals can add clinically useful information. Confirmation of the early relapse window provides a practical framework for optimizing surveillance, while chemoresistance and hematologic toxicity establish a foundation for future response-based, individualized treatment strategies.

5 | Limitations

This study has several limitations. First, the single-center retrospective design and modest sample size limit generalizability and reduce the precision of subgroup estimates, particularly for advanced-stage and high-risk categories. Second, evolution of SIOP-based treatment details and radiotherapy indications over the 2010–2020 period may have introduced clinical heterogeneity that could not be fully controlled in retrospective analyses.

Third, the absence of molecular biomarker data (e.g., 1p/16q loss, WT1, MYCN) restricted analyses to clinical and classical histopathologic variables and precluded exploration of molecular mechanisms

underlying chemoresistance and relapse. In addition, response assessment during pre-operative therapy while response assessment relied on standardized ultrasonography rather than MRI, this reflects a radiation-sparing, real-world workflow essential for long-term survivorship. Minimizing radiation exposure is a critical strategy to reduce late effects, as secondary malignancies are significantly higher in radiotherapy-exposed cohorts compared to those managed with surgery and chemotherapy alone

Finally, follow-up duration varied across patients and, although missingness for key variables was low, these factors may introduce uncertainty in disease-free survival estimates and limit the precision of relapse-timing characterization in some cases.

Despite these limitations, the study has several strengths, including systematic reporting of 10-year real-world outcomes for unilateral Wilms tumor from a tertiary pediatric oncology center; parallel evaluation of stage, SIOP risk stratification, treatment response, and hematologic toxicity parameters within a single cohort; confirmation of an early relapse window based on temporal relapse analysis; and attention to practical surgical quality indicators such as lymph node sampling in relation to staging and relapse risk.

6 | Conclusion

This 10-year study presents one of the first large-scale real-world datasets for unilateral Wilms tumor from the Caucasus region, demonstrating that systematic adherence to SIOP protocols can achieve survival rates (88–90%) approaching high-income country reference values, such as the 5-year OS of 93.6% recently reported in the 2024 SEER database analysis. Our findings confirm the presence of an intensive early relapse period (≤ 24 months). This supports the concept of conditional survival, where the likelihood of long-term survival increases significantly once this milestone is reached.

Specifically, we identified chemotherapy resistance defined by ultrasound and host hematologic responses, particularly thrombocytopenia, as strong, “clinically actionable” prognostic determinants. In the absence of advanced molecular profiling, these clinical signals can serve as vital substitutes for aggressive biological factors recently associated with chemotherapy resistance and reduced disease-free survival, such as 1q gain or novel variants in the ALPK2, C16orf96, and PRKDC genes. In the future, risk classification in resource-limited settings should transition toward integrating absolute blastem volume (> 20–50 mL) as a definitive predictor of poor prognosis, consistent with current SIOP UMBRELLA strategies. Overall, this study demonstrates that integrating treatment response dynamics and easily measurable clinical parameters into a standard framework is a practical and effective way to close the global survival gap in pediatric oncology.

Finally, future multicenter prospective studies, including harmonized pathology and molecular characterization, are needed to validate these observations and to refine response-based, individualized strategies for chemoresistant subgroups. Overall, integrating treatment-response and readily measurable clinical parameters into risk assessment offers a practical pathway toward more targeted follow-up and risk-adapted management within SIOP-guided care.

Declarations

Author Contributions

R.M. and G.I. conceptualized and designed the study.
G.Ə. contributed to patient care and provided clinical input during data interpretation.
A.N. performed and reviewed radiologic assessments, including ultrasound-based evaluation of chemotherapy response.
G.I. and I.B. were responsible for data collection and initial data processing.
R.M., G.I., and I.B. performed the statistical analyses and interpreted the data.
G.I. and I.B. drafted the initial manuscript, and R.M. and R.İ critically revised the manuscript for important intellectual content. S.K.K. performed the statistical analysis and contributed to the interpretation of the results.
All authors reviewed and approved the final version of the manuscript and agreed to its submission.

Ethics Approval

The protocol of this study was approved by the Ethics Committee of the National Oncology Center (Ethics Protocol No.: MOM-2025/47, approval date: 07.10.2024) and was conducted in accordance with the principles of the Declaration of Helsinki. Since the study was retrospective in nature and the data were used in an anonymized manner, written informed consent was not required.

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Data Availability

The data used in this study were obtained from the database of the National Oncology Center. Although the data are not publicly available, the main datasets may be shared upon reasonable request and with the permission of the National Oncology Center.

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Figures

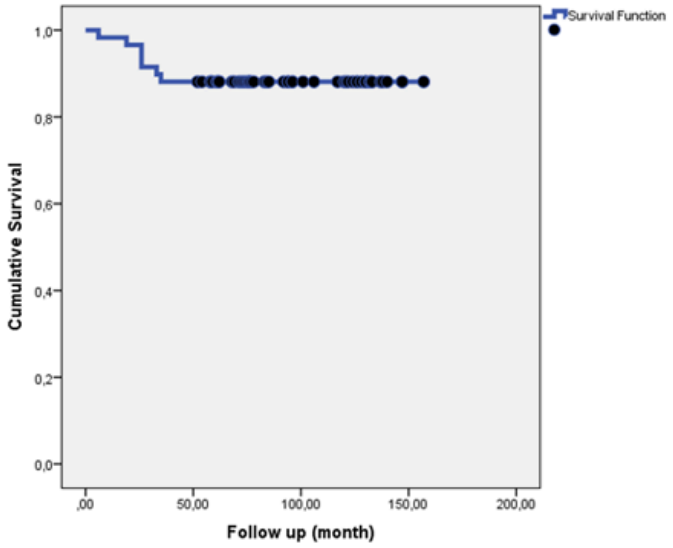


Figure 1A: Mean survival time : 141.27±5.60 month

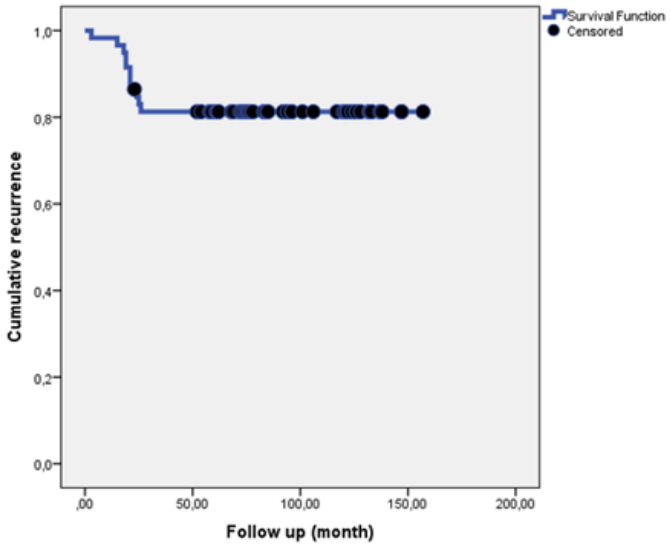


Figure 1B: Mean recurrens time : 131.18±7.03 month

Figure 1

Kaplan–Meier survival outcomes for the entire cohort. (A) Overall survival (OS). **(B)**Disease-free survival (DFS).