



Prediction values of different lymph nodes staging systems for survival of children with Wilms tumor

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Background: Wilms tumor is one of the most common pediatric kidney cancers with poor prognosis. This study aims to explore the predictive values of lymph nodes (LNs), positive lymph node density (LND) and log odds of positive lymph nodes (LODDS) for the 5-year mortality of children with Wilms tumor.

Methods: The cohort study collected the data of 874 participants with Wilms tumor in the Surveillance, Epidemiology, and End Results (SEER) database. The univariate COX proportional risk model was used to explore the possible covariates. The univariate and multivariable COX proportional risk model were employed for exploring the correlations of LNs, LND, and LODDS with the 5-year mortality of Wilms tumor patients. The predictive values of LNs, LND, and LODDS for the 5-year mortality of children with Wilms tumor were evaluated via concordance and 95% confidence interval (CI).

Results: The follow-up time was 5 years, and 804 participants survived in the end. The results delineated that LND >0 [hazard ratio (HR) =1.92, 95% CI: 1.01–3.67] as well as LND ≥0.93 (HR =4.87, 95% CI: 2.42–9.81) were correlated with increased risk of 5-year mortality while LODDS ≥-0.34 (HR =4.09, 95% CI: 2.18–7.65) was linked with elevated risk of 5-year mortality. The concordance of LNs for predicting the 5-year mortality of Wilms tumor patients was 0.623 (95% CI: 0.566–0.681). The concordances of LND, and LODDS for predicting the 5-year mortality of Wilms tumor patients were 0.623 (95% CI: 0.566–0.681) and 0.616 (95% CI: 0.562–0.669).

Conclusions: The predictive value of LODDS for the 5-year mortality of children with Wilms tumor was similar with LNs and LND. The findings might provide a new tool for helping the clinicians identify those with poor prognosis, and timely treatments should be offered to these patients.

Keywords: Wilms tumor; lymph nodes (LNs); positive lymph node density (positive LND); log odds of positive lymph nodes (LODDS)

Submitted Jun 11, 2024. Accepted for publication Sep 29, 2024. Published online Dec 26, 2024.

doi: 10.21037/tcr-24-959

View this article at: <https://dx.doi.org/10.21037/tcr-24-959>

Introduction

Wilms tumor is one of the most common pediatric kidney cancers that represents 6% to 7% of pediatric cancer cases and affects about 0.2 cases per million individuals (1,2). Currently, multimodal strategies have markedly improved the prognoses of patients with Wilms tumor and the 5-year

overall survival (OS) rate can achieve 90% in developed countries through the optimized utilization of current treatment strategies, including chemotherapy, surgery, and radiotherapy (3). The overall prognosis for Wilms tumor is good; however, individuals with diffuse anaplasia (unfavorable histology) or favorable histology experiencing

disease relapse may have a less favorable outcome (4) as well as children with advanced tumors (5) remain to have poor outcomes. In some resource-challenged settings, the OS rate is only 25–53%, which continues to be sub-optimal (6).

Lymph node (LN) involvement is previously reported to be an important prognostic factor of Wilms tumor (7). A previous study has shown that the OS and event-free survival of children with stage III Wilms tumor with positive LNs are poor (8). Positive LNs or positive lymph node density (LND) have been proposed for risk stratification of Wilms tumor and they are found to have certain prognostic value (7,9). These are not applicable for Wilms tumor patients without positive LN metastases. On this basis, log odds of positive lymph nodes (LODDS) has been proposed and applied to prognostic stratification of various malignant tumors, which have been identified to have better prognostic value than American Joint Committee on Cancer (AJCC) N stage and LND in colon cancer, thyroid cancer, renal cell carcinoma and other cancers (10–12). At present, the prognostic value of LODDS on Wilms tumor is still elusive. Comparisons of prognostic values of various LN staging systems including LND, LODDS and LNs for children with Wilms tumor is necessary for the management of this disease.

In the present study, the associations of LNs, LND, and LODDS with the 5-year mortality were evaluated and the predictive values of LNs, LND, and LODDS for the 5-year mortality of children with Wilms tumor were assessed using

data from the Surveillance, Epidemiology, and End Results (SEER) database. Subgroup analysis was stratified by SEER stage, laterality, and number of LN dissection. We present this article in accordance with the STROBE reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-24-959/rc>).

Methods

Study design and population

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). In this cohort study, the data of 2,565 participants with Wilms tumor were identified in the SEER database (<https://seer.cancer.gov/seerstat/>). The SEER database, encompassing data from 18 cancer registries across the United States, represents the largest cancer database in the country, covering a substantial 26% of the population (13). The SEER database routinely collects comprehensive data on patient-specific and tumor-specific characteristics, encompassing patients' demographics, primary tumor site, stage at diagnosis, tumor morphology, treatment course, follow-up for vital status, and death cause (14). In our study, patient diagnosed before 2004 or after 2015, aged ≥ 20 years, patients without data on tumor size, positive LNs, or LNs, and those lost follow-up were excluded. Finally, the data of 874 patients were analyzed.

Potential covariates

Age (year), sex (female or male), race (Black, White, other or unknown), laterality (bilateral, left or right), tumor size (mm), SEER stage (distant, localized or regional), examined LNs, positive LNs, chemotherapy (yes or no/unknown), surgery [nephron sparing surgery (NSS), radical nephrectomy (RN), not otherwise specified (NOS) or none] and radiation (yes or no/unknown) were potential covariates analyzed in this study.

Main and outcome variables

LNs, LND and LODDS were main variables in the present study. Patients had positive LNs were grouped in 1, and those without positive LNs were categorized into 0 group. $LND = \text{positive LN}/\text{examined LN}$. $LODDS = \log [(positive LN + 0.5)/(\text{examined LN} - \text{positive LN} + 0.5)]$. The x-tile was applied for binary classification of LND (< 0.03

Highlight box

Key findings

- The predictive value of log odds of positive lymph nodes (LODDS) for the 5-year mortality of children with Wilms tumor was similar with lymph nodes (LNs), and lymph node density.

What is known and what is new?

- LN involvement is previously reported to be an important prognostic factor of Wilms tumor, and LODDS has been proposed and applied to prognostic stratification of colon cancer, thyroid cancer, renal cell carcinoma.
- $LODDS \geq -0.34$ was linked with elevated risk of 5-year mortality, and had good predictive ability for 5-year mortality of children with Wilms tumor.

What is the implication, and what should change now?

- The findings might provide a new tool for helping the clinicians identify those with poor prognosis. Future studies with external data were required to verify the predictive value of LODDS for the prognosis of children with Wilms tumor.

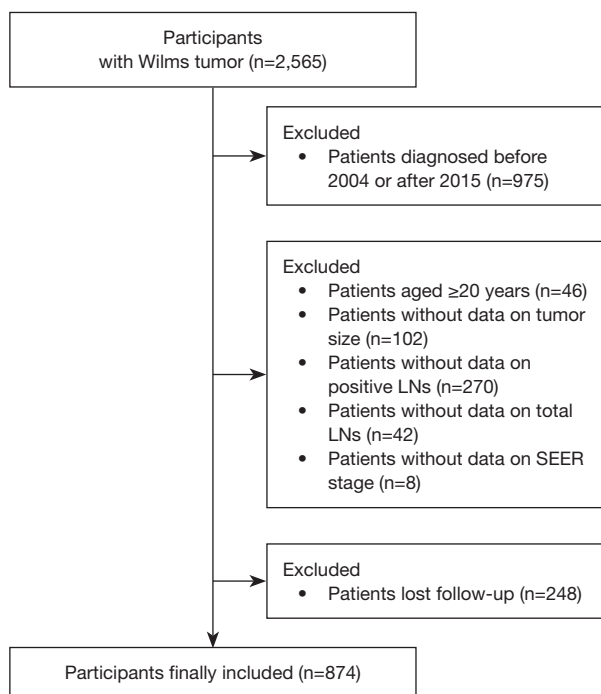


Figure 1 The screen process of the participants. LNs, lymph nodes; SEER, Surveillance, Epidemiology, and End Results.

or ≥ 0.03) and LODDS (< -0.34 or ≥ -0.34), and three-way classification of LND (0, > 0 to < 0.93 or ≥ 0.93), and LODDS (< -1.61 or -1.61 to < -0.34 or ≥ -0.34) based on the minimum P value method.

Whether the Wilms tumor patients survived or died within 5 years was the outcome in our study. The follow-up time was 5 years until 2021.

Statistical analysis

The continuous variables of normal distribution were presented by mean \pm standard deviation (SD), and the *t*-test of two samples was adopted. The data of non-normal distribution were represented as M (Q₁, Q₃), and the rank sum test of two independent samples was applied. The categorical data were shown as n (%) and comparisons between groups were subjected to Chi-squared test or Fisher's exact probability method. The univariate COX proportional risk model was used to explore the possible covariates. The univariate and multivariable COX proportional risk model were employed for explore the associations of LNs, LND, and LODDS with the 5-year mortality of Wilms tumor patients. In Model 1, no covariate was adjusted, and in Model 2, age, sex, laterality,

SEER stage and radiation were adjusted. Subgroup analysis was stratified by SEER stage, laterality, and number of LN dissection. The predictive values of LNs, LND, and LODDS for the 5-year mortality of children with Wilms tumor were evaluated via concordance and 95% confidence interval (CI). Data analysis was subjected to SAS 9.4 (SAS Institute Inc., Cary, USA). $P < 0.05$ was set as statistical difference.

Results

The characteristics of alive or dead Wilms tumor patients within 5 years

In total, 2,565 patients with Wilms tumor were found in the SEER database. Patient diagnosed before 2004 or after 2015 ($n=975$), aged ≥ 20 years ($n=46$), patients without data on tumor size ($n=102$), positive LNs ($n=270$), LNs ($n=42$), or SEER stage ($n=8$), and those lost follow-up ($n=248$) were excluded. Finally, 874 patients were included. The screen process of participants is presented in *Figure 1*.

According to *Table 1*, there were 804 patients survived and 70 patients died. the mean age of alive patients was lower than dead patients (3.34 *vs.* 4.07 years). The percentage of participants with positive LNs in the alive group was lower than the dead group (17.41% *vs.* 42.86%). The percentages of patients in the alive group in different LND and LODDS groups were different from the dead group. The percentages of patients received radiation in the alive group was lower than the dead group (47.18% *vs.* 64.29%).

Covariates related to the 5-year mortality of patients with Wilms tumor

The data from univariate COX proportional risk model depicted that age [hazard ratio (HR) =1.07, 95% CI: 1.01–1.15], right (HR =0.40, 95% CI: 0.16–0.97), distant SEER stage (HR =2.11, 95% CI: 1.25–3.56), localized SEER stage (HR =0.38, 95% CI: 0.19–0.76), and radiation (HR =1.96, 95% CI: 1.20–3.19) were covariates related to the 5-year mortality of patients with Wilms tumor (*Table 2*).

Associations of LNs, LND, and LODDS with the 5-year mortality of Wilms tumor patients

According to the results in *Table 3*, patients with positive LNs (HR =3.33, 95% CI: 2.08–5.35), LND ≥ 0.03 (HR =3.33, 95% CI: 2.08–5.35) and LODDS ≥ -0.34 (HR =4.49, 95% CI: 2.73–7.40) might be related to increased 5-year

Table 1 Comparisons of characteristics of Wilms tumor patients alive or dead within 5 years

Variables	Total (n=874)	Alive (n=804)	Dead (n=70)	Statistics	P
Age, years, mean ± SD	3.40±2.82	3.34±2.78	4.07±3.16	t=-2.08	0.04
Sex, n (%)				$\chi^2=0.562$	0.45
Female	462 (52.86)	428 (53.23)	34 (48.57)		
Male	412 (47.14)	376 (46.77)	36 (51.43)		
Race, n (%)				-	0.38
Black	152 (17.39)	136 (16.92)	16 (22.86)		
Other	49 (5.61)	44 (5.47)	5 (7.14)		
Unknown	10 (1.14)	9 (1.12)	1 (1.43)		
White	663 (75.86)	615 (76.49)	48 (68.57)		
Laterality, n (%)				$\chi^2=3.749$	0.15
Bilateral	39 (4.46)	33 (4.10)	6 (8.57)		
Left	439 (50.23)	401 (49.88)	38 (54.29)		
Right	396 (45.31)	370 (46.02)	26 (37.14)		
Tumor size, mm, M (Q ₁ , Q ₃)	110.00 (80.00, 132.00)	110.00 (80.00, 130.00)	116.00 (75.00, 139.00)	Z=1.015	0.31
SEER stage, n (%)				$\chi^2=32.043$	<0.001
Distant	206 (23.57)	172 (21.39)	34 (48.57)		
Localized	376 (43.02)	364 (45.27)	12 (17.14)		
Regional	292 (33.41)	268 (33.33)	24 (34.29)		
Examined lymph node, M (Q ₁ , Q ₃)	4.00 (2.00, 8.00)	4.00 (2.00, 8.00)	3.50 (2.00, 7.00)	Z=-1.403	0.16
Positive lymph node, M (Q ₁ , Q ₃)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 2.00)	Z=5.232	<0.001
LNs, n (%)				$\chi^2=26.609$	<0.001
0	704 (80.55)	664 (82.59)	40 (57.14)		
1	170 (19.45)	140 (17.41)	30 (42.86)		
Binary classification					
LND, n (%)				$\chi^2=26.609$	<0.001
<0.03	704 (80.55)	664 (82.59)	40 (57.14)		
≥0.03	170 (19.45)	140 (17.41)	30 (42.86)		
LODDS, n (%)				$\chi^2=38.727$	<0.001
<-0.34	780 (89.24)	733 (91.17)	47 (67.14)		
≥-0.34	94 (10.76)	71 (8.83)	23 (32.86)		
Three-way classification					
LND, n (%)				$\chi^2=29.001$	<0.001
0	704 (80.55)	664 (82.59)	40 (57.14)		
>0 to <0.93	134 (15.33)	116 (14.43)	18 (25.71)		
≥0.93	36 (4.12)	24 (2.99)	12 (17.14)		

Table 1 (continued)

Table 1 (continued)

Variables	Total (n=874)	Alive (n=804)	Dead (n=70)	Statistics	P
LODDS, n (%)				$\chi^2=42.092$	<0.001
<-1.61	493 (56.41)	470 (58.46)	23 (32.86)		
-1.61 to <-0.34	287 (32.84)	263 (32.71)	24 (34.29)		
≥-0.34	94 (10.76)	71 (8.83)	23 (32.86)		
Chemotherapy, n (%)				$\chi^2=0.018$	0.89
No/unknown	66 (7.55)	61 (7.59)	5 (7.14)		
Yes	808 (92.45)	743 (92.41)	65 (92.86)		
Surgery, n (%)				-	0.42
NOS	54 (6.18)	47 (5.85)	7 (10.00)		
NSS	28 (3.20)	26 (3.23)	2 (2.86)		
None	1 (0.11)	1 (0.12)	0 (0.00)		
RN	791 (90.50)	730 (90.80)	61 (87.14)		
Radiation, n (%)				$\chi^2=7.540$	0.006
None/unknown	446 (51.44)	421 (52.82)	25 (35.71)		
Yes	421 (48.56)	376 (47.18)	45 (64.29)		
Time, month, M (Q ₁ , Q ₃)	60.0 (60.0, 60.0)	60.0 (60.0, 60.0)	21.5 (13.0, 32.0)	Z=-29.512	<0.001

LNs: 0, negative; 1, positive. Z, Mann-Whitney U test; χ^2 , Chi-squared test; -, Fisher exact. SD, standard deviation; M, median; Q₁, 1st quartile; Q₃, 3rd quartile; SEER, Surveillance, Epidemiology, and End Results; LNs, lymph nodes; LND, lymph node density; LODDS, log odds of positive lymph nodes; NOS, not otherwise specified; NSS, nephron sparing surgery; RN, radical nephrectomy.

mortality risk. After adjusting for age, laterality, SEER stage, and radiation, increased 5-year mortality risk in children with Wilms tumor was observed in positive LNs (HR =2.64, 95% CI: 1.48–4.69), LND ≥ 0.03 (HR =2.64, 95% CI: 1.48–4.69) and LODDS ≥ -0.34 (HR =3.20, 95% CI: 1.84–5.57). We further categorized LND and LODDS into three groups. The data depicted that $0 < \text{LND} < 0.93$ (HR =1.92, 95% CI: 1.01–3.67) as well as LND ≥ 0.93 (HR =4.87, 95% CI: 2.42–9.81) were correlated with increased risk of 5-year mortality while LODDS ≥ -0.34 (HR =4.09, 95% CI: 2.18–7.65) was related to heightened 5-year mortality risk (Table 3). Patients with positive LNs (Figure 2), LND ≥ 0.03 (Figure 3) and LODDS ≥ -0.34 (Figure 4) were associated with poor survival probability.

The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients

The concordance of LNs for predicting the 5-year mortality of Wilms tumor children was 0.623 (95% CI: 0.566–0.681).

The concordances of LND, and LODDS in two-category data for predicting the 5-year mortality of Wilms tumor patients were 0.623 (95% CI: 0.566–0.681) and 0.616 (95% CI: 0.562–0.669), respectively. When divided LND, and LODDS into three groups, the concordances for predicting the 5-year mortality of Wilms tumor patients were 0.631 (95% CI: 0.572–0.690) and 0.660 (95% CI: 0.596–0.724), respectively. No significant difference was found in the concordances of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients (Table 4).

Subgroup analysis of the predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients

In those with regional SEER stage, the predictive values of LNs, LND, and LODDS for the 5-year mortality were 0.656 (95% CI: 0.559–0.753), 0.656 (95% CI: 0.559–0.753) and 0.626 (95% CI: 0.528–0.723). The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms

Table 2 Potential covariates associated with the 5-year mortality of patients with Wilms tumor

Variables	β	S.E	χ^2	HR (95% CI)	P
Age	0.071	0.035	4.211	1.07 (1.01–1.15)	0.040
Sex					
Female				Ref	
Male	0.178	0.239	0.556	1.20 (0.75–1.91)	0.46
Race					
Black				Ref	
Other	–0.023	0.512	0.002	0.98 (0.36–2.67)	0.96
Unknown	–0.001	1.031	0.000	1.00 (0.13–7.53)	0.99
White	–0.384	0.289	1.770	0.68 (0.39–1.20)	0.18
Laterality					
Bilateral				Ref	
Left	–0.630	0.439	2.059	0.53 (0.23–1.26)	0.15
Right	–0.917	0.453	4.104	0.40 (0.16–0.97)	0.04
Tumor size	–0.000	0.002	0.001	1.00 (1.00–1.00)	0.98
SEER stage					
Distant	0.748	0.267	7.863	2.11 (1.25–3.56)	0.005
Localized	–0.970	0.354	7.528	0.38 (0.19–0.76)	0.006
Regional				Ref	
Examined lymph node	–0.041	0.025	2.633	0.96 (0.91–1.01)	0.11
Positive lymph node	0.192	0.045	17.926	1.21 (1.11–1.32)	<0.001
Chemotherapy					
No/unknown				Ref	
Yes	0.057	0.464	0.015	1.06 (0.43–2.63)	0.90
Surgery					
NOS	0.561	0.399	1.977	1.75 (0.80–3.83)	0.16
NSS	–0.080	0.719	0.012	0.92 (0.23–3.78)	0.91
None	–9.980	519.25	0.000	–	0.99
RN				Ref	
Radiation					
None/unknown				Ref	
Yes	0.672	0.249	7.252	1.96 (1.20–3.19)	0.007

–, insufficient frequency to fit. S.E, standard error; HR, hazard ratio; CI, confidence interval; Ref, reference; SEER, Surveillance, Epidemiology, and End Results; NOS, not otherwise specified; NSS, nephron sparing surgery; RN, radical nephrectomy.

Table 3 Associations of LNs, LND, and LODDS with the 5-year mortality of Wilms tumor patients

Variables	Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P
LN				
0	Ref		Ref	
1	3.33 (2.08–5.35)	<0.001	2.64 (1.48–4.69)	<0.001
Binary classification				
LND				
<0.03	Ref		Ref	
≥0.03	3.33 (2.08–5.35)	<0.001	2.64 (1.48–4.69)	<0.001
LODDS				
<-0.34	Ref		Ref	
≥-0.34	4.49 (2.73–7.40)	<0.001	3.20 (1.84–5.57)	<0.001
Three-way classification				
LND				
0	Ref		Ref	
>0 to <0.93	2.51 (1.44–4.37)	0.001	1.92 (1.01–3.67)	0.049
≥0.93	6.63 (3.48–12.65)	<0.001	4.87 (2.42–9.81)	<0.001
LODDS				
<-1.61	Ref		Ref	
-1.61 to <-0.34	1.82 (1.03–3.23)	0.040	1.71 (0.97–3.04)	0.07
≥-0.34	5.84 (3.28–10.41)	<0.001	4.09 (2.18–7.65)	<0.001

Model 1: unadjusted univariate COX proportional risk model; Model 2: multivariable COX proportional risk model adjusted for age, sex, laterality, SEER stage, and radiation. LNs, lymph nodes; LND, lymph node density; LODDS, log odds of positive lymph nodes; HR, hazard ratio; CI, confidence interval; Ref, reference; SEER, Surveillance, Epidemiology, and End Results.

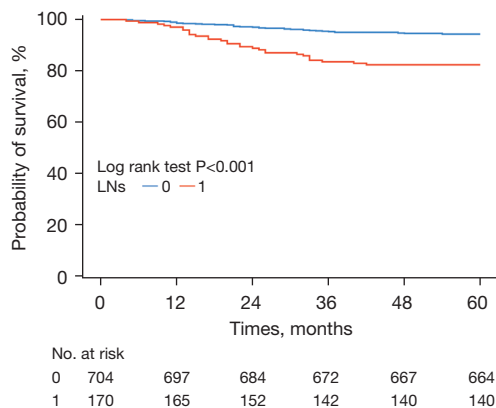


Figure 2 The Kaplan-Meier survival curves of patients in different LNs groups. 0, negative; 1, positive. LNs, lymph nodes.

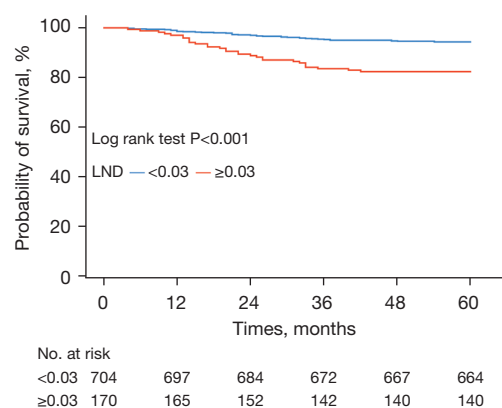


Figure 3 The Kaplan-Meier survival curves of patients in different LND groups. LND, lymph node density.

tumor patients with distant SEER stage. The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor children with tumor in left kidney were 0.627 (95% CI: 0.548–0.706), 0.627 (95% CI: 0.548–0.706)

and 0.595 (95% CI: 0.523–0.667). The predictive value of LODDS for the 5-year mortality of Wilms tumor patients with tumor in right kidney was 0.657 (95% CI: 0.565–0.749), which was higher than LNs [area under the curve

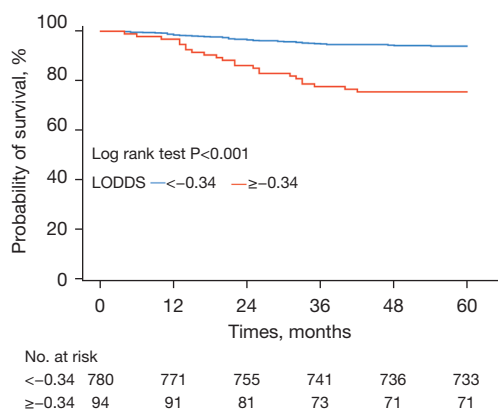


Figure 4 The Kaplan–Meier survival curves of patients in different LODDS groups. LODDS, log odds of positive lymph nodes.

Table 4 The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients

Predictors	Concordance (95% CI)
LNs	0.623 (0.566–0.681)
Binary classification	
LND	0.623 (0.566–0.681)
LODDS	0.616 (0.562–0.669)
Three-way classification	
LND	0.631 (0.572–0.690)
LODDS	0.660 (0.596–0.724)

LNs, lymph nodes; LND, lymph node density; LODDS, log odds of positive lymph nodes; CI, confidence interval.

(AUC) =0.631 (95% CI: 0.538–0.724)] and LND [AUC =0.631 (95% CI: 0.538–0.724)]. The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients with examined LNs ≥ 10 were 0.637 (95% CI: 0.502–0.773), 0.637 (95% CI: 0.502–0.773) and 0.597 (95% CI: 0.486–0.707). The predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients with examined LNs < 10 were 0.621 (95% CI: 0.558–0.684), 0.621 (95% CI: 0.558–0.684) and 0.619 (95% CI: 0.558–0.680) (Table 5).

Discussion

Positive LNs, LND ≥ 0.03 and LODDS ≥ -0.34 were related to elevated 5-year mortality risk of Wilms tumor children. The predictive value of LODDS for the 5-year mortality of

children with Wilms tumor was similar with LNs and LND. Subgroup analysis revealed that the predictive value of LODDS for the 5-year mortality of Wilms tumor children with tumor in right kidney was higher than LNs and LND. The findings might provide a tool for identifying those with high risk of mortality within 5 years especially for patients without positive LNs, and offer chance for timely treatments for these patients to improve the outcomes.

LODDS is a logical transformation formula stratifying differences in survival between patients at a single stage of the disease based on pathological LN data, even if the number of positive LNs is 0 (15). LODDS is considered to be a prognostic metric for lymph-node metastasis in different cancers like medullary thyroid carcinoma (16), non-small cell lung cancer (17), and urothelial bladder cancer (18). The classification of LN status via LODDS has been found as a reliable prognostic index with a good value to identify those with high risk of prognosis, irrespective of LN status and count. In our study, higher LODDS was correlated with heightened 5-year mortality risk in patients with Wilms tumor. LODDS showed good predictive value for 5-year mortality in patients with Wilms tumor. The findings suggested that LODDS can assist clinicians in identifying whether patients with clinically aggressive tumors are at a higher risk of 5-year mortality, regardless of nodal positivity. This information has the potential to guide treatment decisions for these patients.

The prognosis evaluation of patients with Wilms tumor traditionally relies on the involvement of nodal disease, including the total number of positive LNs, by clinicians (19). Adequate LNs sampling is regarded to be conducive for the assessment of prognosis (20,21). Honeyman *et al.* revealed that LNs involvement was related to the possibility of relapse and OS of patients with Wilms tumor (22). A study of Stewart *et al.* depicted that the sampling LNs was independently correlated with the recurrence rate and survival for Wilms tumor patients (23). Additionally, in a review of the National Cancer Database (NCDB), observed LND were identified to be linked to the OS of patients with LN-positive favorable histology Wilms tumor (24). Another study also indicated that LND was identified to an independent risk factor for the prognosis of children with Wilms tumor (25). In the present study, patients with positive LNs or higher LND were related to the increase of 5-year mortality risk in children with Wilms tumor. The predictive values of LNs and LND were good. The predictive value of LODDS for the 5-year mortality of children with Wilms tumor was similar with that of LNs

Table 5 Subgroup analysis of the predictive values of LNs, LND, and LODDS for the 5-year mortality of Wilms tumor patients

Models	SEER stage [concordance (95% CI)]		Laterality [concordance (95% CI)]			Examined [concordance (95% CI)]	
	Regional	Distant	Bilateral	Left	Right	≥10	<10
Predictors							
LNs	0.656 (0.559–0.753)	0.549 (0.465–0.633)	0.556 (0.420–0.692)	0.627 (0.548–0.706)	0.631 (0.538–0.724)	0.637 (0.502–0.773)	0.621 (0.558–0.684)
Binary classification							
LND	0.656 (0.559–0.753)	0.549 (0.465–0.633)	0.556 (0.420–0.692)	0.627 (0.548–0.706)	0.631 (0.538–0.724)	0.637 (0.502–0.773)	0.621 (0.558–0.684)
LODDS	0.626 (0.528–0.723)	0.597 (0.517–0.677)	0.556 (0.420–0.692)	0.595 (0.523–0.667)	0.657 (0.565–0.749) ^{a,b}	0.597 (0.486–0.707)	0.619 (0.558–0.680)
Three-way classification							
LND	0.668 (0.566–0.770)	0.564 (0.471–0.657)	0.582 (0.451–0.713)	0.632 (0.552–0.713)	0.639 (0.542–0.735)	0.646 (0.506–0.785)	0.627 (0.562–0.692)
LODDS	0.645 (0.535–0.755)	0.669 (0.585–0.753)	0.627 (0.406–0.847)	0.645 (0.561–0.729)	0.681 (0.571–0.792)	0.673 (0.537–0.809)	0.657 (0.586–0.729)

^a, statistically different compared with LNS; ^b, statistically different compared with LND. LNs, lymph nodes; LND, lymph node density; LODDS, log odds of positive lymph nodes; SEER, Surveillance, Epidemiology, and End Results; CI, confidence interval.

and LND. In addition, the predictive value of LODDS for the 5-year mortality of Wilms tumor patients with tumor in right kidney was higher than that of LNs and LND. These implied that LODDS could also be applied for identifying Wilms tumor patients at high risk of poor prognosis. LODDS is not affected by the number of LNs sent for examination, which can further stratify patients with no LNs (26). The pediatric surgeons and urologists should evaluate more accurate interventions and treatments for patients who are identified to have high risk of poor prognosis. If necessary, surgical management could be applied, and in the future, the development of metaverse including 3D virtual models and robotic surgery will allow surgeons to explore surgical fields of Wilms tumor, which may improve the prognosis of these patients (27).

Several limitations were identified in our study. Firstly, the site and dose of radiation were not included in SEER database, which might be related to Wilms tumor patients' prognosis. Secondly, International Society of Paediatric Oncology (SIOP) and Children's Oncology Group (COG) staging are important for evaluating the prognosis and treatment strategies for children with Wilms tumor, but these data were not recorded and evaluated by SEER. This necessitates further well-designed studies to substantiate the findings of this present study.

Conclusions

We found that positive LNs, higher LND and LODDS were related to increased risk of 5-year mortality of patients with Wilms tumor. The predictive value of LODDS for the 5-year mortality of children with Wilms tumor was similar with LNs and LND. The LODDS might help the clinicians identify those with poor prognosis, regardless of nodal positivity, and timely interventions should be provided to these patients to improve their prognosis. However, some important variables were not analyzed, and future studies with external data were required to verify the predictive value of LODDS for the prognosis of children with Wilms tumor.

Acknowledgments

Funding: This project was supported by Hainan Province Clinical Medical Center (QWYH202175).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-24-959/rc>

Peer Review File: Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-24-959/prf>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-24-959/coif>). All authors report that this project was supported by Hainan Province Clinical Medical Center (QWYH202175). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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References

1. Elgenidy A, Afifi AM, Gad EF, et al. Survival characteristics of Wilms Tumor, a reference developed from a longitudinal cohort study. *Ital J Pediatr* 2024;50:141.
2. Alijani B, Abbaspour E, Karimzadghagh S, et al. First incidence of extrarenal wilms tumor within the spinal canal in the adult population: a novel case report and literature review. *BMC Urol* 2024;24:119.
3. Mapelli M, Zagni P, Ferrara R, et al. Unexpected Huge Prevalence of Intracardiac Extension of Wilms Tumor-A Single Center Experience from a Ugandan Hospital. *Children (Basel)* 2022;9:743.
4. Jablonowski CM, Gil HJ, Pinto EM, et al. TERT Expression in Wilms Tumor Is Regulated by Promoter Mutation or Hypermethylation, WT1, and N-MYC. *Cancers (Basel)* 2022;14:1655.
5. Liu BH, Liu GB, Zhang BB, et al. Tumor Suppressive Role of MUC6 in Wilms Tumor via Autophagy-Dependent β -Catenin Degradation. *Front Oncol* 2022;12:756117.
6. Cunningham ME, Klug TD, Nuchtern JG, et al. Global Disparities in Wilms Tumor. *J Surg Res* 2020;247:34-51.
7. You H, Yang J, Liu Q, et al. The impact of the lymph node density on overall survival in patients with Wilms' tumor: a SEER analysis. *Cancer Manag Res* 2018;10:671-7.
8. Ehrlich PF, Anderson JR, Ritchey ML, et al. Clinicopathologic findings predictive of relapse in children with stage III favorable-histology Wilms tumor. *J Clin Oncol* 2013;31:1196-201.
9. Walker JP, Johnson JS, Eguchi MM, et al. Factors affecting lymph node sampling patterns and the impact on survival of lymph node density in patients with Wilms tumor: a Surveillance, Epidemiology, and End Result (SEER) database review. *J Pediatr Urol* 2020;16:81-8.
10. Cai H, Xu T, Zhuang Z, et al. Value of the log odds of positive lymph nodes for prognostic assessment of colon mucinous adenocarcinoma: Analysis and external validation. *Cancer Med* 2021;10:8542-57.
11. Tang J, Jiang S, Gao L, et al. Construction and Validation of a Nomogram Based on the Log Odds of Positive Lymph Nodes to Predict the Prognosis of Medullary Thyroid Carcinoma After Surgery. *Ann Surg Oncol* 2021;28:4360-70.
12. Zhou W, Huang C, Yuan N. Prognostic nomograms based on log odds of positive lymph nodes for patients with renal cell carcinoma: A retrospective cohort study. *Int J Surg* 2018;60:28-40.
13. Chierigo F, Flammia RS, Sorce G, et al. The association of type and number of high-risk criteria with cancer-specific mortality in prostate cancer patients treated with radical prostatectomy. *Curr Urol* 2024;18:128-32.
14. Wu YL, Hong YY, Zhan HL, et al. Axillary lymph node removal in de novo metastatic breast cancer. *Gland Surg* 2024;13:1214-28.
15. Li T, Yang Y, Wu W, et al. Prognostic implications of ENE and LODDS in relation to lymph node-positive colorectal cancer location. *Transl Oncol* 2021;14:101190.
16. Cao ZX, Weng X, Huang JS, et al. Prognostic value of LODDS in medullary thyroid carcinoma based on competing risk model and propensity score matching analysis. *Updates Surg* 2022;74:1551-62.
17. Wang Q, Wang S, Sun Z, et al. Evaluation of log odds of positive lymph nodes in predicting the survival of patients with non-small cell lung cancer treated with neoadjuvant therapy and surgery: a SEER cohort-based study. *BMC Cancer* 2022;22:801.
18. Salari A, Ghahari M, Nowroozi A, et al. Log Odds of Positive Lymph Nodes (LODDS) as an Independent Predictor of Overall Survival Following Radical Cystectomy in Urothelial Bladder Cancer: Time to

- Rethink Conventional Node Staging. *Clin Genitourin Cancer* 2023;21:e175-81.
19. Jayakumar TK, Pathak M, Sinha A. Outcomes of event-free survival in patients with Wilms tumor undergoing preoperative chemotherapy. Analysis of lymph-node yield in a single-center cohort. *J Pediatr Urol* 2021;17:228-9.
 20. Qureshi SS, Bhagat M, Kazi M, et al. Standardizing lymph nodal sampling for Wilms tumor: A feasibility study with outcomes. *J Pediatr Surg* 2020;55:2668-75.
 21. Saltzman AF, Smith DE, Gao D, et al. How many lymph nodes are enough? Assessing the adequacy of lymph node yield for staging in favorable histology wilms tumor. *J Pediatr Surg* 2019;54:2331-5.
 22. Honeyman JN, Rich BS, McEvoy MP, et al. Factors associated with relapse and survival in Wilms tumor: a multivariate analysis. *J Pediatr Surg* 2012;47:1228-33.
 23. Stewart CL, Bruny JL. Maximizing lymph node retrieval during surgical resection of Wilms tumor. *Eur J Pediatr Surg* 2015;25:109-12.
 24. Saltzman AF, Carrasco A Jr, Amini A, et al. Patterns of lymph node sampling and the impact of lymph node density in favorable histology Wilms tumor: An analysis of the national cancer database. *J Pediatr Urol* 2018;14:161.e1-8.
 25. Tan X, Wang J, Tang J, et al. A Nomogram for Predicting Cancer-Specific Survival in Children With Wilms Tumor: A Study Based on SEER Database and External Validation in China. *Front Public Health* 2022;10:829840.
 26. Zhou YY, Du XJ, Zhang CH, et al. Comparison of three lymph node staging schemes for predicting the outcome in patients with small bowel adenocarcinoma: A population-based cohort and international multicentre cohort study. *EBioMedicine* 2019;41:276-85.
 27. Della Corte M, Clemente E, Checcucci E, et al. Pediatric urology Metaverse. *Surgeries* 2023;4:325-34.

Cite this article as: Chen S, Wan Z, Hu S, Bu W, Lu Y, Zhao Z. Prediction values of different lymph nodes staging systems for survival of children with Wilms tumor. *Transl Cancer Res* 2024;13(12):6688-6698. doi: 10.21037/tcr-24-959