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A Prognostic Nomogram Based on Log Odds of Positive Lymph Nodes for Patients with Gastroenteropancreatic Neuroendocrine Tumors

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Abstract: *Objective:* To explore the prognostic value of log odds of positive lymph nodes (LODDS) in patients with gastroenteropancreatic neuroendocrine tumors (GEPNET) and to develop nomograms based on LODDS for predicting 1-year, 3-year, and 5-year overall survival (OS) and cancer-specific survival (CSS). *Methods:* This retrospective cohort study was based on the Surveillance, Epidemiology, and End Results (SEER) Program. Demographic data, clinical data, and survival status were extracted, with endpoints of OS and CSS. Multivariate Cox proportional hazards regression analysis assessed predictors associated with OS and CSS, with hazard ratios (HRs) and 95% confidence intervals (CIs) evaluated. Nomogram performance was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC). *Results:* A total of 1,673 patients were included and divided into a training set (n = 1,172) and a testing set (n = 501). Multivariate Cox proportional hazards regression analyses identified LODDS as an independent prognostic factor for OS (HR = 1.79, 95% CI: 1.44–2.24) and CSS (HR = 1.81, 95% CI: 1.41–2.31). The OS and CSS nomograms, developed from multivariate Cox regression analyses, showed good performance, with AUCs of 0.858, 0.878, and 0.852 for predicting 1-year, 3-year, and 5-year OS, and AUCs of 0.859, 0.887, and 0.865 for 1-year, 3-year, and 5-year CSS in the testing set. The nomograms are accessible online (OS: https://zhmte.shinyapps.io/DynNomapp/; CSS: https://zhmty.shinyapps.io/DynNomapp/). *Conclusions:* LODDS serves as an independent prognostic factor in GEPNET. Online nomograms based on LODDS demonstrated effective performance in predicting OS and CSS in GEPNET patients, providing a convenient tool for clinical application.

Keywords: Log odds of positive lymph nodes; Online dynamitic nomograms; Overall survival; Cancer-specific survival

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1. Introduction

Gastroenteropancreatic neuroendocrine tumors (GEPNET) are a group of genetically diverse neoplasms

arising from neuroendocrine system secretory cells, accounting for 62%–67% of neuroendocrine tumors [1]. The incidence of GEPNET has risen in recent decades, with a reported six-fold increase in age-adjusted annual incidence between 1973 and 2012 in the United States [2]. Generally, patients with early-stage GEPNET have a favorable prognosis; however, many are diagnosed at a metastatic stage, and not all cases are eligible for curative resection [3]. Due to the heterogeneous and complex biological behaviors of these tumors, predicting the prognosis of GEPNET patients remains challenging [4].

Lymph node status is considered a critical prognostic factor in GEPNET [5]. The tumor-node-metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC) relies on the number of positive regional lymph nodes; however, the accuracy of pN staging may be compromised by the limited number of lymph nodes retrieved [6,7]. Additionally, negative lymph nodes have been reported to influence survival outcomes in gastrointestinal cancers and neuroendocrine tumors [8-10]. To address these limitations, the log odds of positive lymph nodes (LODDS) were proposed as a prognostic factor, defined as the logarithm of the ratio of positive to negative lymph nodes. LODDS has been identified as an effective prognostic indicator in small bowel neuroendocrine tumors [10]; however, its prognostic role in GEPNET remains unreported. Accurate prognostic predictions in GEPNET may assist clinicians in recommending treatments, stratifying participants, and counseling patients on disease severity. Currently, high-quality prognostic risk assessment models for GEPNET are still lacking [11].

A nomogram is a visual tool that can simplify complex factors into a single, user-friendly model to predict event probabilities, providing clinicians with a more accurate prognosis assessment [12]. This study aims to develop an online nomogram based on LODDS to predict the prognosis of GEPNET patients.

2. Methods

2.1. Data source

This retrospective cohort study was conducted using data from the 2000–2019 Surveillance, Epidemiology, and End Results (SEER) Program (https://seer.cancer.gov/), which provides U.S. cancer statistics and is supported by the National Cancer Institute (NCI). The SEER database is publicly available and de-identified, thus exempting this study from patient informed consent and Ethics Committee approval from the Fourth Affiliated Hospital of Nanjing Medical University.

2.2. Study population

Patients diagnosed with neuroendocrine tumors in the 2000–2019 SEER database, aged ≥ 18 years, and with primary sites in the stomach, pancreas, colon, or rectum were included in this study. Exclusion criteria were as follows: (1) patients with other cancers or secondary cancers, (2) those with incomplete data (e.g., missing TNM stage, number of dissected lymph nodes, or number of positive lymph nodes), (3) GEPNET confirmed by autopsy or death certificate, (4) missing data on the specific cause of death, (5) missing survival time data, and (6) missing data on tumor differentiation and tumor size. The follow-up period concluded on November 31, 2019, with a median duration of 56.00 (14.00, 87.00) months.

Neuroendocrine tumors were identified using the International Classification of Diseases for Oncology (ICD-O-3) by site recode and histology/behavior codes: 8013/3 (large cell neuroendocrine carcinoma), 8153/3 (gastrinoma, malignant), 8240/3 (carcinoid tumor, NOS), 8241/3 (Enterochromaffin cell carcinoid), 8242/3

(Enterochromaffin-like cell tumor, malignant), 8246/3 (neuroendocrine carcinoma, NOS), 8249/3 (atypical carcinoid tumor), and 8574/3 (adenocarcinoma with neuroendocrine differentiation).

2.3. Data collection

Demographic, clinical, and survival data were collected. Demographic data included age (<60 years and ≥60 years), sex (male and female), race (black, white, and other), and marital status (married, single, divorced, widowed, unknown). Clinical data included tumor size, primary site (stomach, pancreas, colon, rectum), T stage (T1, T2, T3, T4, other), N stage (N1, N2, other), M stage (M0, M1, other), tumor differentiation (well, moderate, poor, undifferentiated, unknown), laterality (no, yes), surgery (no, local, radical), radiotherapy (no, yes), and chemotherapy (no, yes).

2.4. Log odds of positive lymph nodes (LODDS)

LODDS is defined as the logarithm of the ratio between the number of positive lymph nodes and the number of negative lymph nodes and is calculated as follows: log((number of positive lymph nodes + 0.5) / (number of dissected lymph nodes - number of positive lymph nodes + 0.5)) [13]. Based on a previous study, LODDS was divided into three groups (< -1.36, -1.36 to -0.53, > -0.53) [13].

2.5. Outcomes

The two study endpoints were overall survival (OS) and cancer-specific survival (CSS). OS was defined as the time from diagnosis to death from any cause or to the last follow-up. CSS was defined as the time from diagnosis to death specifically caused by GEPNET. The 1-year, 3-year, and 5-year OS and CSS were observed.

2.6. Statistical analysis

Continuous variables with non-normal distributions were presented as medians and quartiles [M (Q1, Q3)], and differences between groups were analyzed using the Wilcoxon rank sum test. Categorical variables were shown as counts and percentages [n (%)], with chi-square or Fisher's exact tests used to assess group differences. Kaplan-Meier (KM) survival curves were generated and compared using the log-rank test.

Univariate and multivariate survival analyses were conducted using the Cox proportional hazards model, with hazard ratios (HR) and 95% confidence intervals (CIs) calculated. Variables with statistical significance in univariate analysis were included in multivariate Cox regression to identify independent prognostic factors for nomogram development. The dataset was split into training and testing sets in a 7:3 ratio. Nomogram performance was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC), with calibration plots showing the relationship between predicted probabilities and actual outcomes.

The ROC curve was generated using Python 3.7.4 (Python Software Foundation, Delaware, USA). Nomograms, KM curves, and calibration plots were created using R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). A two-tailed *P*-value of < 0.05 was considered statistically significant.

3. Results

3.1. Patient selection and characteristics

A total of 1,673 patients were extracted from the SEER database for this study. The eligible patients were divided into a training set (n = 1,172) and a testing set (n = 501) at a 7:3 ratio (**Figure 1**). Of these patients, 48.54% were aged ≥ 60 years, 49.85% were male, 79.32% were of white race, and 61.69% were married. No statistically significant differences were observed between the training and testing sets in terms of age, sex, race, marital status, tumor size, primary site, T stage, N stage, M stage, tumor differentiation, laterality, surgery, radiotherapy, chemotherapy, survival time, LODDS, OS, or CSS (**Table 1**).

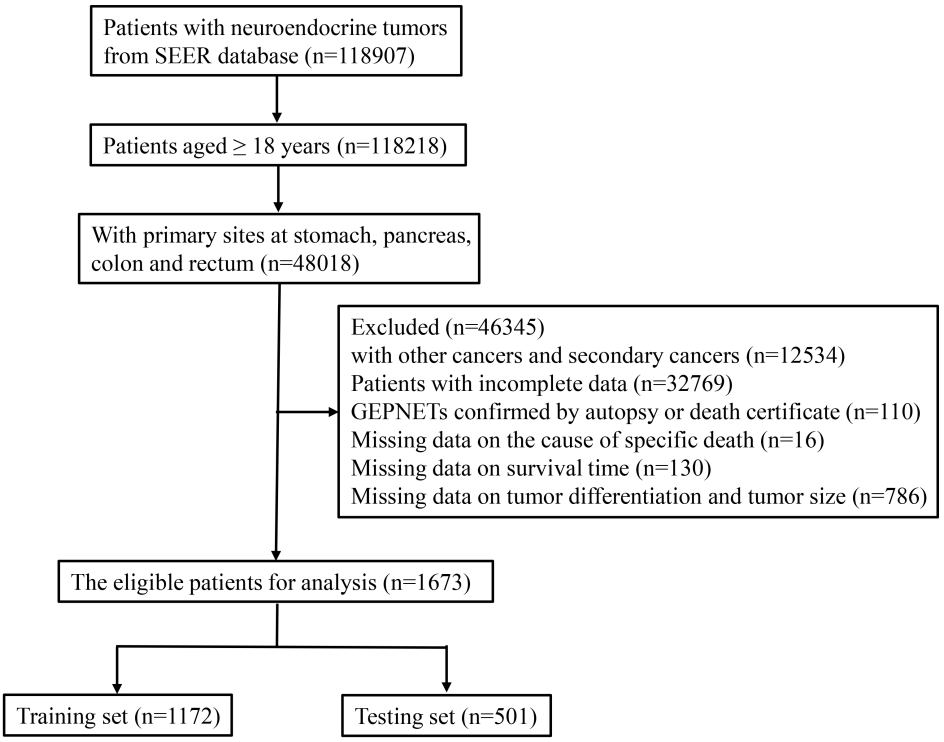

Figure 1. Study selection process

Table 1. Comparison of characteristics between training set and testing set

Variables	Total (n = 1,673)	Training set (n = 1,172)	Testing set (n = 501)	*P*
Age, years, *n* (%)				0.533
< 60	861 (51.46)	609 (51.96)	252 (50.30)	
≥ 60	812 (48.54)	563 (48.04)	249 (49.70)	
Sex, *n* (%)				0.323
Male	834 (49.85)	575 (49.06)	259 (51.70)	
Female	839 (50.15)	597 (50.94)	242 (48.30)	
Race, *n* (%)				0.925
White	1,327 (79.32)	927 (79.10)	400 (79.84)	
Black	220 (13.15)	155 (13.23)	65 (12.97)	
Other	126 (7.53)	90 (7.68)	36 (7.19)	

Table 1 (Continued)

Variables	Total (*n* = 1,673)	Training set (*n* = 1,172)	Testing set (*n* = 501)	*P*
Marital status, *n* (%)				0.594
Married	1,032 (61.69)	731 (62.37)	301 (60.08)	
Divorced	153 (9.15)	99 (8.45)	54 (10.78)	
Single	264 (15.78)	188 (16.04)	76 (15.17)	
Widowed	148 (8.85)	101 (8.62)	47 (9.38)	
Unknown	76 (4.54)	53 (4.52)	23 (4.59)	
Tumor size, cm, M (Q_1, Q_3)	4.00 (2.50,6.00)	4.00 (2.50,6.00)	4.00 (2.80,6.00)	0.262
Primary site, *n* (%)				0.567
Stomach	127 (7.59)	94 (8.02)	33 (6.59)	
Pancreas	610 (36.46)	434 (37.03)	176 (35.13)	
Colon	844 (50.45)	580 (49.49)	264 (52.69)	
Rectum	92 (5.50)	64 (5.46)	28 (5.59)	
T stage, *n* (%)				0.425
T1	123 (7.35)	95 (8.11)	28 (5.59)	
T2	312 (18.65)	216 (18.43)	96 (19.16)	
T3	900 (53.80)	626 (53.41)	274 (54.69)	
T4	328 (19.61)	229 (19.54)	99 (19.76)	
Other	10 (0.60)	6 (0.51)	4 (0.80)	
N stage, *n* (%)				0.485
N1	1,409 (84.22)	984 (83.96)	425 (84.83)	
N2	256 (15.30)	181 (15.44)	75 (14.97)	
Other	8 (0.48)	7 (0.60)	1 (0.20)	
M stage, *n* (%)				0.794
M0	1,096 (65.51)	764 (65.19)	332 (66.27)	
M1	571 (34.13)	403 (34.39)	168 (33.53)	
Other	6 (0.36)	5 (0.43)	1 (0.20)	
Tumor differentiation, n (%)				0.496
Well	674 (40.29)	480 (40.96)	194 (38.72)	
Moderate	256 (15.30)	173 (14.76)	83 (16.57)	
Poor	413 (24.69)	297 (25.34)	116 (23.15)	
Undifferentiated	158 (9.44)	104 (8.87)	54 (10.78)	
Unknown	172 (10.28)	118 (10.07)	54 (10.78)	
Laterality, n (%)				0.434
Yes	7 (0.42)	4 (0.34)	3 (0.60)	
No	1,666 (99.58)	1,168 (99.66)	498 (99.40)	

Table 1 (Continued)

Variables	Total (*n* = 1,673)	Training set (*n* = 1,172)	Testing set (*n* = 501)	*P*
Surgery, n (%)				0.715
No	322 (19.25)	227 (19.37)	95 (18.96)	
Local	551 (32.93)	392 (33.45)	159 (31.74)	
Radical	800 (47.82)	553 (47.18)	247 (49.30)	
Radiotherapy, n (%)				0.071
Yes	112 (6.69)	70 (5.97)	42 (8.38)	
No	1,561 (93.31)	1,102 (94.03)	459 (91.62)	
Chemotherapy, n (%)				0.612
Yes	460 (27.50)	318 (27.13)	142 (28.34)	
No	1213 (72.50)	854 (72.87)	359 (71.66)	
Survival time, months, M (Q_1, Q_3)	56.00 (14.00,87.00)	55.00 (13.00,86.00)	58.00 (14.00,88.00)	0.417
LODDS, n (%)				0.481
< -1.36	564 (33.71)	388 (33.11)	176 (35.13)	
-1.36 to -0.53	387 (23.13)	267 (22.78)	120 (23.95)	
> -0.53	722 (43.16)	517 (44.11)	205 (40.92)	
OS, n (%)				0.658
Survival	831 (49.67)	578 (49.32)	253 (50.50)	
Death	842 (50.33)	594 (50.68)	248 (49.50)	
CSS, n (%)				0.828
No specific death	955 (57.08)	667 (56.91)	288 (57.49)	
Specific death	718 (42.92)	505 (43.09)	213 (42.51)	

Abbreviations: CSS, cancer specific survival, LODDS, log odds of positive lymph nodes; OS, overall survival.

Note: Continuous data in abnormal distribution were presented as median and quartile [M (Q1, Q3)], and compared using the Wilcoxon rank sum test. Categorical variables were shown as numbers and percentages [*n* (%)], and compared using the chi-squared test or Fisher's exact test.

3.2. Prognostic factors for OS and CSS

The prognostic factors for OS and CSS were assessed using univariate and multivariate Cox proportional hazards regression analyses. Independent prognostic factors for OS included age (HR = 1.92, 95% CI: 1.61–2.30), marital status (widowed: HR = 1.34, 95% CI: 1.04–1.74), tumor size (HR = 1.03, 95% CI: 1.01–1.06), primary site (pancreas: HR = 0.70, 95% CI: 0.49–0.99), N stage (other: HR = 2.92, 95% CI: 1.31–6.54), M stage (M1: HR = 2.12, 95% CI: 1.76–2.54; other: HR = 2.89, 95% CI: 1.05–8.00), tumor differentiation (poor: HR = 4.27, 95% CI: 3.31–5.50; undifferentiated: HR = 5.71, 95% CI: 4.19–7.79; unknown: HR = 1.91, 95% CI: 1.39–2.62), surgery (radical: HR = 0.55, 95% CI: 0.40–0.77), and LODDS (> -0.53: HR = 1.79, 95% CI: 1.44–2.24) (**Table 2**). Independent prognostic factors for CSS mirrored those for OS, with the exception of the primary site (**Table 3**). Kaplan-Meier (KM) curves indicated significant differences in OS and CSS among the three LODDS groups (**Figure 2**).

Table 2. Cox regression for analyzing the prognostic factors for OS of GEPNET patients in the training set

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age				
<60	Ref		Ref	
≥60	2.27 (1.92–2.68)	< 0.001	1.92 (1.61–2.30)	< 0.001
Sex				
Male	Ref		-	
Female	1.06 (0.90–1.25)	0.464		
Race				
White	Ref		-	
Black	0.86 (0.67–1.10)	0.217		
Other	0.78 (0.56–1.08)	0.133		
Marital status				
Married	Ref		Ref	
Divorced	1.41 (1.06–1.87)	0.017	1.11 (0.83–1.49)	0.468
Single	1.06 (0.84–1.33)	0.629	1.15 (0.90–1.47)	0.252
Widowed	2.35 (1.84–3.01)	< 0.001	1.34 (1.04–1.74)	0.026
Unknown	0.99 (0.65–1.51)	0.962	0.98 (0.64–1.51)	0.923
Tumor size	1.10 (1.08–1.12)	< 0.001	1.03 (1.01–1.06)	0.026
Primary site				
Stomach	Ref		Ref	
Pancreas	0.50 (0.38–0.67)	< 0.001	0.70 (0.49–0.99)	0.045
Colon	0.84 (0.64–1.11)	0.220	1.00 (0.74–1.35)	0.985
Rectum	0.77 (0.51–1.16)	0.207	0.80 (0.52–1.24)	0.318
T stage				
T1	Ref		Ref	
T2	1.69 (1.04–2.73)	0.033	1.08 (0.66–1.78)	0.750
T3	2.82 (1.81–4.38)	< 0.001	1.06 (0.67–1.69)	0.805
T4	5.46 (3.47–8.60)	< 0.001	1.35 (0.83–2.21)	0.227
Other	2.68 (0.92–7.81)	0.071	2.42 (0.81–7.21)	0.112
N stage				
N1	Ref		Ref	
N2	3.69 (3.07–4.45)	< 0.001	1.26 (1.00–1.60)	0.053
Other	5.79 (2.74–12.24)	< 0.001	2.92 (1.31–6.54)	0.009
M stage				
M0	Ref		Ref	
M1	2.99 (2.54–3.52)	< 0.001	2.12 (1.76–2.54)	< 0.001

Table 2 (Continued)

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Other	2.48 (0.92–6.68)	0.071	2.89 (1.05–8.00)	0.040
Tumor differentiation				
Well	Ref		Ref	
Moderate	1.43 (1.05–1.94)	0.023	1.17 (0.85–1.59)	0.336
Poor	6.70 (5.40–8.32)	< 0.001	4.27 (3.31–5.50)	< 0.001
Undifferentiated	9.04 (6.87–11.90)	< 0.001	5.71 (4.19–7.79)	< 0.001
Unknown	2.20 (1.62–2.98)	< 0.001	1.91 (1.39–2.62)	< 0.001
Laterality				
Yes	Ref		-	
No	0.45 (0.17–1.21)	0.113		
Surgery				
No	Ref		Ref	
Local	1.08 (0.85–1.36)	0.549	0.78 (0.57–1.05)	0.096
Radical	1.36 (1.09–1.69)	0.006	0.55 (0.40–0.77)	< 0.001
Radiotherapy				
Yes	Ref		Ref	
No	0.59 (0.45–0.79)	< 0.001	0.88 (0.64–1.20)	0.422
Chemotherapy				
Yes	Ref		Ref	
No	0.33 (0.28–0.39)	< 0.001	0.92 (0.75–1.12)	0.382
LODDS				
< -1.36	Ref		Ref	
-1.36 to -0.53	1.32 (1.03–1.69)	0.028	1.14 (0.88–1.48)	0.324
> -0.53	2.59 (2.12–3.16)	< 0.001	1.79 (1.44–2.24)	< 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; LODDS, log odds of positive lymph nodes; OS, overall survival; Ref, Reference.

Table 3. Cox regression for analyzing the prognostic factors for CSS of GEPNET patients in the training set

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age				
< 60	Ref		Ref	
≥ 60	2.01 (1.68–2.40)	< 0.001	1.71 (1.41–2.07)	< 0.001
Sex				
Male	Ref		-	
Female	1.02 (0.86–1.22)	0.819		

Table 3 (Continued)

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Race				
White	Ref		-	
Black	0.82 (0.63–1.08)	0.163		
Other	0.87 (0.62–1.22)	0.419		
Marital status				
Married	Ref		Ref	
Divorced	1.50 (1.11–2.02)	0.008	1.18 (0.87–1.60)	0.293
Single	1.06 (0.82–1.36)	0.675	1.12 (0.86–1.46)	0.408
Widowed	2.18 (1.66–2.86)	< 0.001	1.28 (0.96–1.71)	0.098
Unknown	1.11 (0.72–1.72)	0.627	1.07 (0.68–1.66)	0.780
Tumor size	1.11 (1.09–1.12)	< 0.001	1.03 (1.01–1.06)	0.017
Primary site				
Stomach	Ref		Ref	
Pancreas	0.50 (0.36–0.68)	< 0.001	0.69 (0.47–1.02)	0.061
Colon	0.84 (0.62–1.12)	0.235	0.97 (0.70–1.35)	0.855
Rectum	0.85 (0.55–1.30)	0.456	0.83 (0.52–1.31)	0.415
T stage				
T1	Ref		Ref	
T2	1.76 (1.00–3.10)	0.051	1.06 (0.59–1.89)	0.847
T3	3.40 (2.02–5.72)	< 0.001	1.16 (0.67–2.00)	0.596
T4	6.57 (3.86–11.18)	< 0.001	1.45 (0.82–2.56)	0.205
Other	2.87 (0.83–9.90)	0.096	2.60 (0.74–9.19)	0.138
N stage				
N1	Ref		Ref	
N2	4.09 (3.36-4.97)	< 0.001	1.33 (1.03-1.71)	0.027
Other	7.11 (3.36-15.05)	< 0.001	3.11 (1.37-7.06)	0.007
M stage				
M0	Ref		Ref	
M1	3.49 (2.92–4.17)	< 0.001	2.35 (1.93–2.87)	< 0.001
Other	2.47 (0.79–7.71)	0.121	2.67 (0.83–8.61)	0.100
Tumor differentiation				
Well	Ref		Ref	
Moderate	1.76 (1.26–2.47)	< 0.001	1.45 (1.03–2.04)	0.033
Poor	8.06 (6.30–10.32)	< 0.001	4.99 (3.76–6.63)	< 0.001

Table 3 (Continued)

Variables	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Undifferentiated	11.39 (8.44–15.37)	< 0.001	6.89 (4.91–9.66)	< 0.001
Unknown	2.38 (1.67–3.37)	< 0.001	2.08 (1.44–2.99)	< 0.001
Laterality				
Yes	Ref		-	
No	0.79 (0.20–3.18)	0.744		
Surgery				
No	Ref		Ref	
Local	1.14 (0.88–1.48)	0.317	0.80 (0.57–1.11)	0.179
Radical	1.36 (1.07–1.73)	0.013	0.53 (0.37–0.76)	< 0.001
Radiotherapy				
Yes	Ref		Ref	
No	0.53 (0.40–0.71)	< 0.001	0.81 (0.59–1.13)	0.212
Chemotherapy				
Yes	Ref		Ref	
No	0.30 (0.25–0.35)	< 0.001	0.91 (0.73–1.12)	0.361
LODDS				
< -1.36	Ref		Ref	
-1.36 to -0.53	1.44 (1.10–1.90)	0.008	1.15 (0.86–1.53)	0.345
> -0.53	2.87 (2.30–3.59)	< 0.001	1.81 (1.41–2.31)	< 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; LODDS, log odds of positive lymph nodes; OS, overall survival; Ref, Reference.

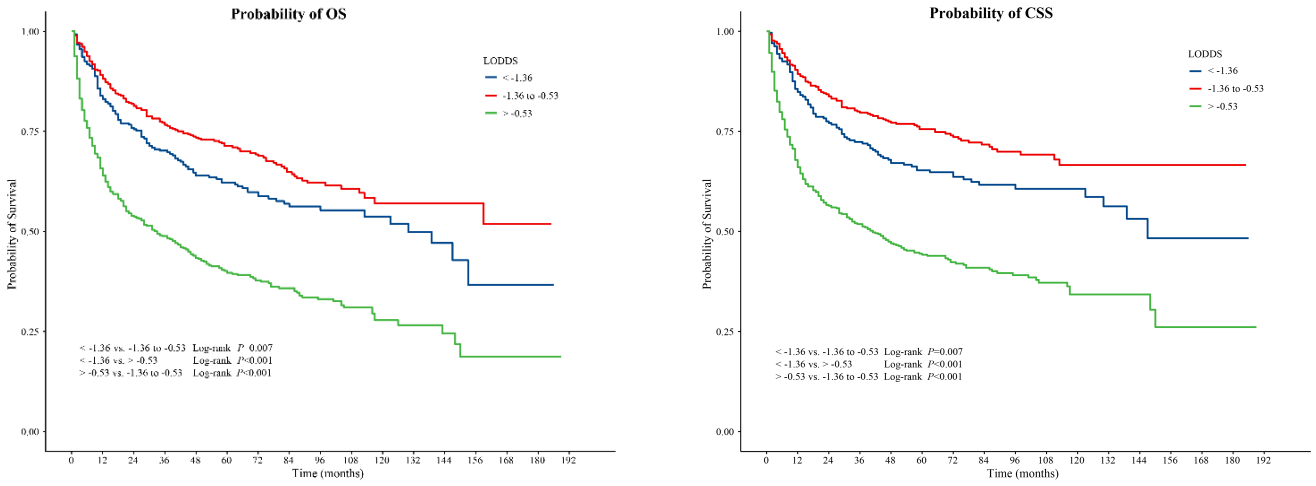

Figure 2. Kaplan-Meier curve of OS **(left)** and OSS **(right)** for GEPNET patients with LODDS value of < -1.36, -1.36 to -0.53, and > -0.53.

3.3. Nomograms

Separate OS and CSS nomograms were developed based on the prognostic factors identified for OS and CSS in the Cox proportional hazards regression analyses (**Figure 3**). For instance, a patient aged <60 years, married, with an 8 cm tumor size, the primary site at the pancreas, N1 stage, M0 stage, well-differentiated tumor, no surgery, and LODDS between -1.36 and -0.53 had a 1-year OS probability of 95.26%, a 3-year OS probability of 90.11%, and a 5-year OS probability of 86.05%. This patient's 1-year, 3-year, and 5-year CSS probabilities were 96.16%, 92.08%, and 89.13%, respectively. Calibration plots demonstrated that the predicted 1-year, 3-year, and 5-year OS and CSS probabilities closely matched the actual outcomes (**Figure 4**). **Figure 5** presents the ROC curves for the nomogram prediction models in both the training and testing sets. The AUCs for predicting 1-year, 3-year, and 5-year OS were 0.889, 0.886, and 0.878 in the training set and 0.858, 0.878, and 0.852 in the testing set, respectively. For CSS prediction, the AUCs were 0.887, 0.886, and 0.870 in the training set and 0.859, 0.887, and 0.865 in the testing set. These AUC values indicated good discriminative ability of the nomogram prediction models. Online access to the nomograms for OS and CSS has been established (OS: https://zhmte.shinyapps.io/DynNomapp/; CSS: https://zhmty.shinyapps.io/DynNomapp/).

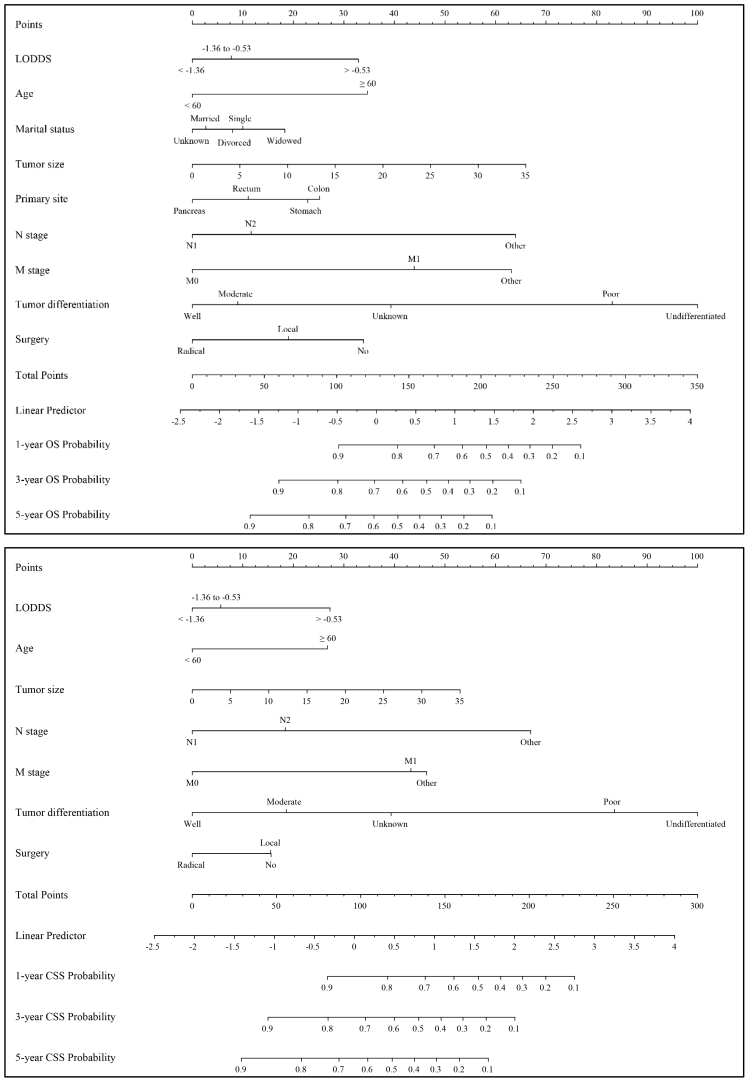

Figure 3. Nomogram predicting the 1-year, 3-year, and 5-year OS **(top)** and CSS **(bottom)** in GEPNET patients

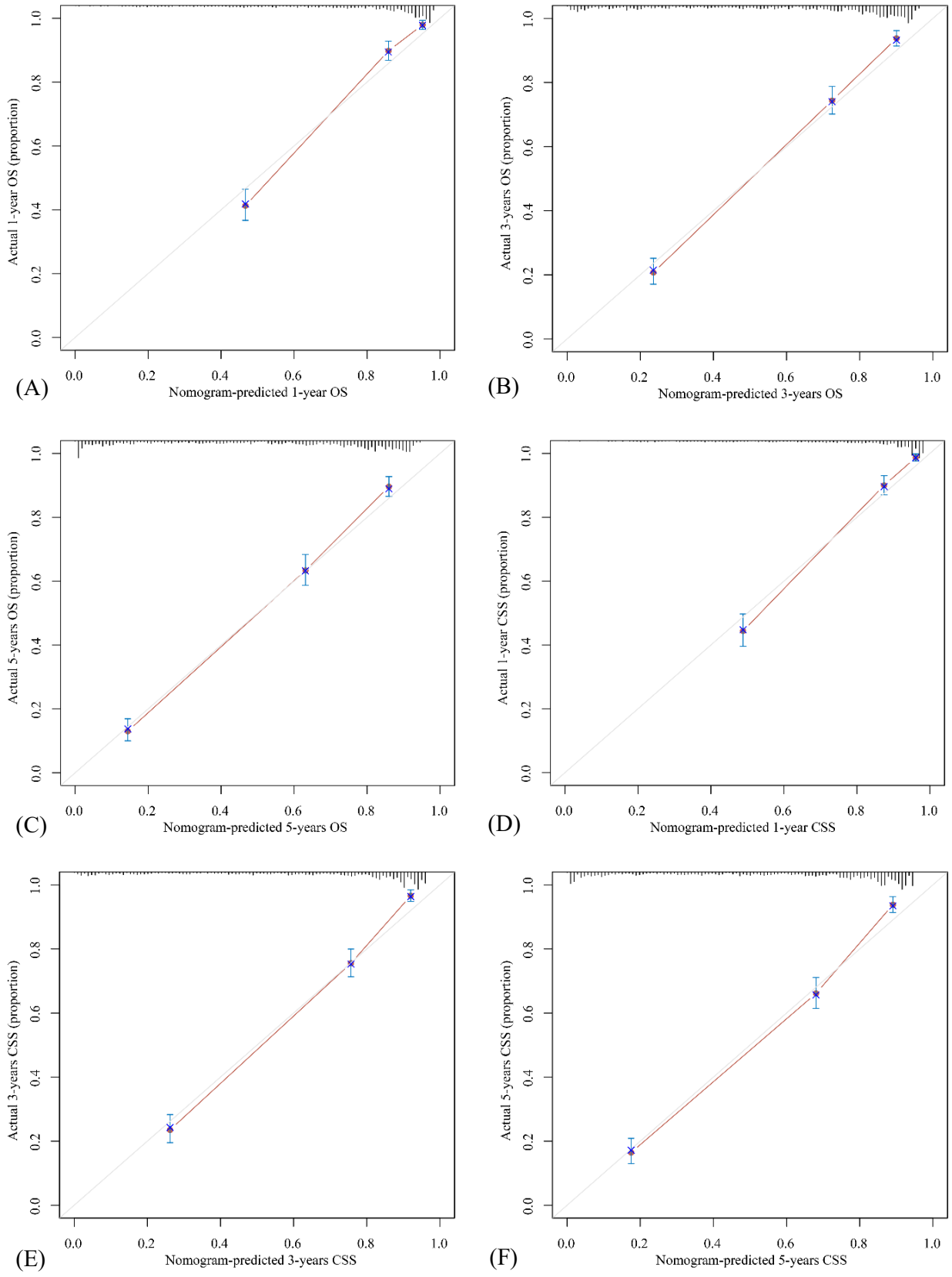

Figure 4. Calibration plots for 1-year OS nomogram **(A)**, 3-year OS nomogram **(B)**, 3-year OS nomogram **(C)**, 1-year CSS nomogram **(D)**, 3-year CSS nomogram **(E)**, and 5-year CSS nomogram **(F)** in the training set

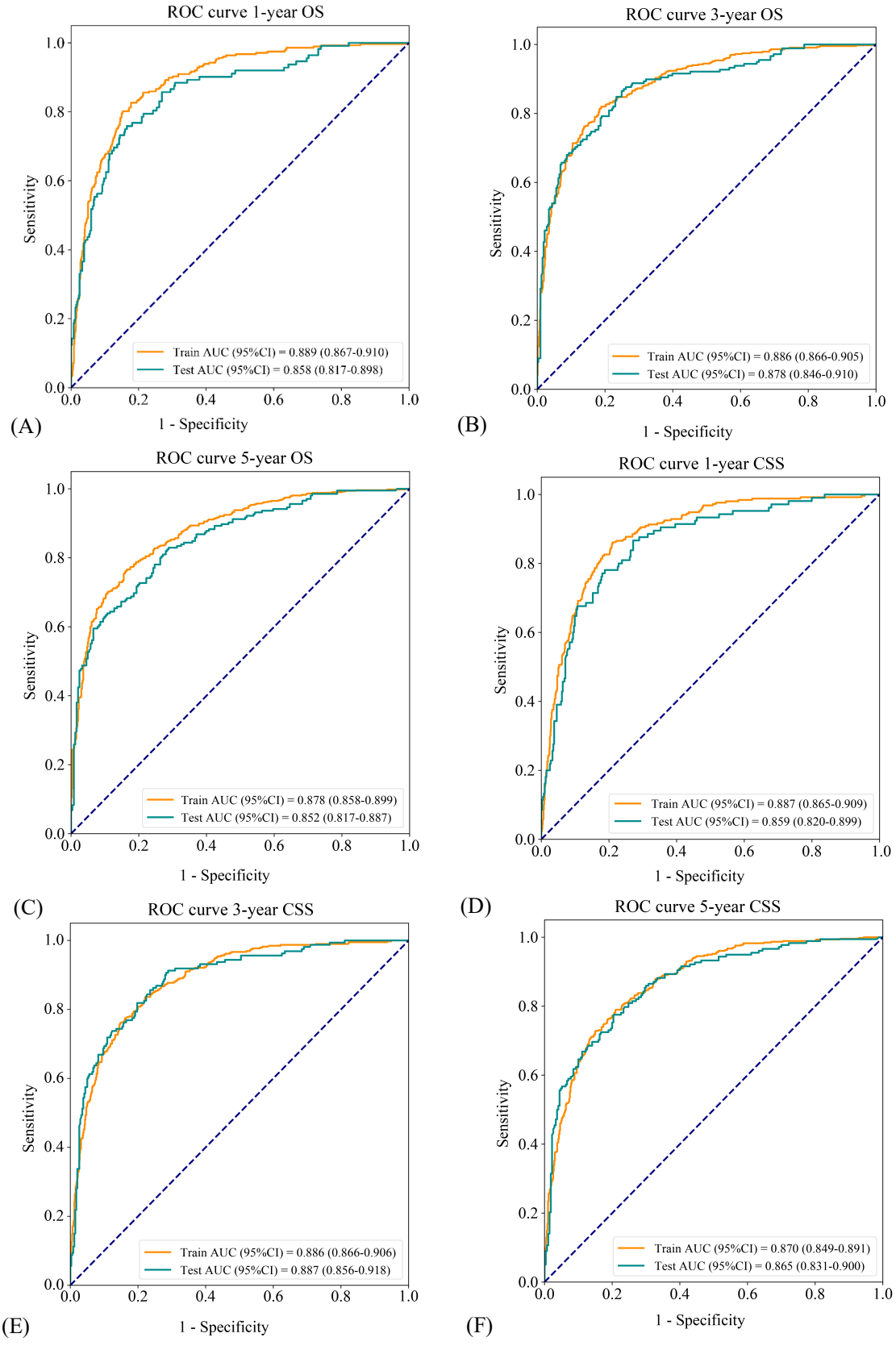

Figure 5. ROC curves for 1-year OS nomogram **(A)**, 3-year OS nomogram **(B)**, 3-year OS nomogram **(C)**, 1-year CSS nomogram **(D)**, 3-year CSS nomogram **(E)**, and 5-year CSS nomogram **(F)** in the training set and testing set

4. Discussion

The incidence of GEPNET has significantly increased in recent decades; however, predicting the prognosis of GEPNET remains challenging in clinical practice due to the heterogeneous outcomes [2,4]. Determining appropriate treatment based on patient prognosis continues to be a challenge for clinicians. This study found that LODDS was independently associated with the prognosis of GEPNET patients. The nomogram based on LODDS performed well in predicting OS and CSS for these patients and is available online, providing a convenient and practical tool for clinicians.

Lymph node status is a significant factor in the prognosis of GEPNET patients and an important consideration for clinicians [5]. While AJCC N staging is currently the most widely used method, it has limitations: it considers only the number of positive lymph nodes, disregarding the total lymph node count, which is also an independent prognostic factor [6,7,14]. Researchers have proposed alternative parameters to evaluate lymph node status, including lymph node ratio and LODDS [15,16]. Although the lymph node ratio accounts for both total and positive lymph nodes, patients with similar ratios may have vastly different prognoses, as some ratios may indicate all non-metastatic or all metastatic nodes [17]. LODDS, as a novel lymph node classification, overcomes the limitations of lymph node ratio, improving the accuracy of prognostic prediction. Studies have reported that LODDS provides superior predictive value compared to AJCC N staging and lymph node ratio [10]. In small bowel neuroendocrine tumor patients, LODDS has been effective for prognosis prediction [10]. Additional studies have supported the effectiveness of LODDS in predicting outcomes for patients with gastric, colon, rectal, and pancreatic cancers [18-20]. This study identified LODDS as an independent prognostic factor for GEPNET, underscoring its importance in evaluating prognosis for these patients.

Previous studies have demonstrated the predictive utility of nomograms for OS in GEPNET [21,22]. These studies highlighted that consistent and specific nomograms are both effective and accurate for predicting the prognosis of GEPNET patients [21,22]. However, these studies did not explore nomograms' predictive ability for CSS, assess lymph node status in GEPNET patients, or develop user-friendly online dynamic nomograms. The current study addresses these limitations by developing an LODDS-based nomogram to predict GEPNET prognosis. Accessible through online platforms, these nomograms allow simple calculation of 1-year, 3-year, and 5-year OS and CSS probabilities by adding the points corresponding to each patient's matching factors. The AUCs for the 1-year, 3-year, and 5-year OS and CSS predictions were all greater than 0.8, demonstrating the strong performance of these nomograms in predicting GEPNET prognosis. Moreover, calibration curves confirmed excellent consistency for predicting OS and CSS across the three time points, providing a reliable and discriminative prognostic evaluation for GEPNET patients. Based on the calculated total score from the nomogram, clinicians may recommend tailored guidance and treatment options, potentially adjusting care according to patients' life expectancy.

This study has several strengths. First, it used data extracted from the SEER database, which contains a large and representative sample from the United States. Second, it identified the prognostic role of LODDS in GEPNET and developed online dynamic nomograms based on LODDS, offering a user-friendly tool for predicting OS and CSS in these patients. However, the study has some limitations. First, the data were retrospectively collected, which introduces inherent selection bias. Second, information on specific surgeries, incisal edge status, and chemotherapy timing, which may impact prognosis, was unavailable due to limitations within the SEER database. Additionally, the external validation of the nomograms requires further verification.

Future studies with larger samples and multi-center designs are recommended to further confirm and expand on these findings.

5. Conclusion

In conclusion, this study identified LODDS as an independent prognostic factor for GEPNET, with online dynamic nomograms based on LODDS showing good predictive performance and practical clinical applicability.

Disclosure statement

The authors declare no conflict of interest.

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