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Development and validation of a nomogram to predict lung metastasis in patients with testicular germ cell tumors

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ABSTRACT

Background: Lung metastatic tumor (LM) is one of testicular germ cell tumors' most common metastatic sites. Our study aimed to develop a nomogram for predicting the risk of LM among patients with testicular germ cell tumors (TGCTs).

Methods: Clinicopathological information of 4078 patients with TGCT between 2010 and 2015 was obtained from SEER. Univariate and multivariate logistic regression analyses were performed to identify risk factors for LM, and a nomogram was developed based on these factors. Calibration curves, area under the receiver operating curve (AUC), and decision curve analysis (DCA) were used to evaluate the accuracy and discrimination of the model.

Results: Study participants included 4078 people with TGCTs, including 305 people with LM. They were randomly divided into two groups (training cohort = 2854 and validation cohort = 1224) at a ratio of 7:3. The following variables were incorporated in the nomogram: marital status, tumor histological type, T stage, brain metastasis, liver metastasis, lactate dehydrogenase (LDH), and chemotherapy. Besides, the AUC of it was 0.922 in the training cohort, while was 0.930 in the validation cohort. Training and validation cohort calibrations showed that the nomogram had excellent predictive abilities. DCA suggested it was more clinically relevant than the traditional TN staging.

Conclusion: We have established a nomogram to predict the risk of LM in patients with TGCTs. Doctors and patients can use this nomogram to monitor and identify lung metastasis of tumors through active monitoring and follow-up.

1. Introduction

Testicular cancer is the most common cancer among young men aged 15–34 years [1]. The vast majority of testicular cancers are testicular germ cell tumors (TGCTs), which are histologically divided into seminomas (SGCTs), nonseminomas (NSGCTs), and spermatocyte tumors (<1%) [[2,3]]. While the prognosis is very favorable in a localized stage, with more than 90% of men surviving beyond 5 years, the 5- year survival decreases to 72.5% for distant disease (12% of cases detected) [4]. Distant lymph node metastases

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and lung metastasis are the most common metastases in patients with testicular germ cell tumors [[5,6]]. Patients with lung metastases have poorer overall survival (OS) and cancer-specific survival (CSS) prognosis compared with patients with distant lymph node metastases [5]. Thus, it is significant for clinicians to predict the risk of lung metastasis in patients with testicular germ cell tumors. Regrettably, a majority of studies focused on OS or CSS in those patients [5–8]. Researchers found a panel of miRNAs that distinguishes metastatic SGCTs from non-metastatic SGCTs by Ernst et al. They confirmed three of them by qRT-PCR. A miRNA expression pattern identification seems to indicate the individual metastatic risk of SGCTs with greater precision than what is currently possible [9]. But these molecules are not readily available and expensive. As we all know, conventional cross-sectional imaging, including computed tomography/positron emission tomography and magnetic resonance imaging (MRI), can provide high-resolution images to detect distant metastases in patients with testicular germ cell tumors. As mentioned earlier, the patients belonged to a relatively young cohort and the tumor prognosis was generally good, which meant prolonged follow-up and monitoring. However, for the former, repeated doses of ionizing radiation carry a risk of secondary malignancies during surveillance. For the latter, MRI has not been widely adopted for this indication, likely due to high cost, long examination times, and reduced availability [10]. In a word, a convenient and accurate prediction model is greatly needed by clinicians to predict the risk of lung metastasis in testicular germ cell tumors. In this study, by extracting data on both patient and tumor characteristics from the Surveillance, Epidemiology, and End Results (SEER) database, we developed and validated a clinical prediction model to quantify the risk of lung metastasis for patients with testicular germ cell tumors. Furthermore, our study will facilitate the development of customized treatment options and medical decisions in patients with testicular germ cell tumors.

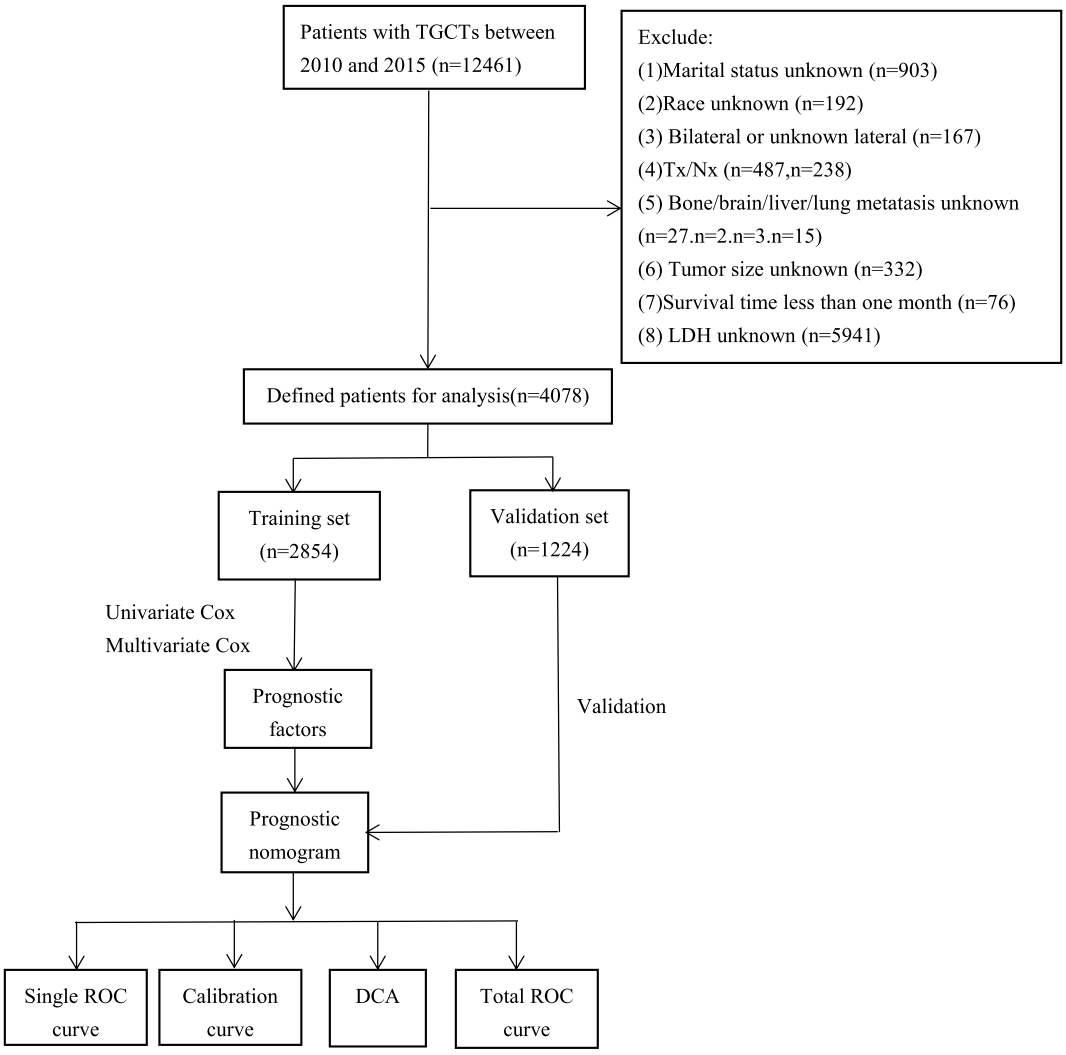

Fig. 1. A schematic overview of the project is presented in this workflow.

2. Methods

2.1. Cohort selection and data Collection

About 28% of cancer registries in the United States are included in SEER. The data used in this study were obtained from SEER Stat 8.4.0. As all SEER database information has been de-identified, institutional review board approval or informed consent was not required for this study. The public database did not collect information on distant metastases until 2010, so we excluded patients diagnosed before 2010. Additionally, patients diagnosed after 2015 are not enrolled to ensure uniform TNM staging information. Among the inclusion criteria were the following: (1) diagnosed between 2010 and 2015, (2) patients with a histologic diagnosis of

Table 1
| Clinicopathological information in patients with testicular germ cell tumors.

Variable	Total(n = 4078)	Training(n = 2584)	Validation(n = 1224)	*P*-value
Marital				0.192
Married	1660 (40.7%)	1181 (41.4%)	479 (39.1%)	
Unmarried	2418 (59.3%)	1673 (58.6%)	745 (60.9%)	
Age				0.145
≤40	3179 (78.0%)	2243 (78.6%)	936 (76.5%)	
>40	899 (22.0%)	611 (21.4%)	288 (23.5%)	
Race				0.022[a]
White	3690 (90.5%)	2565 (89.9%)	1125 (91.9%)	
Black	111 (2.7%)	75 (2.6%)	36 (2.9%)	
Other	277 (6.8%)	214 (7.5%)	63 (5.1%)	
Histology				0.712
SGCT	2019 (49.5%)	1401 (49.1%)	618 (50.5%)	
nSGCT	524 (12.8%)	369 (12.9%)	155 (12.7%)	
Mix-GCT	1535 (37.6%)	1084 (38.0%)	451 (36.8%)	
Laterality				0.519
Left	1916 (47.0%)	1331 (46.6%)	585 (47.8%)	
Right	2162 (53.0%)	1523 (53.4%)	639 (52.2%)	
T stage				0.592
T1-T2	3842 (94.2%)	2693 (94.4%)	1149 (93.9%)	
T3-T4	236 (5.8%)	161 (5.6%)	75 (6.1%)	
N stage				0.674
Node-negative	2995 (73.4%)	2102 (73.7%)	893 (73.0%)	
Node-positive	1083 (26.6%)	752 (26.3%)	331 (27.0%)	
Radiotherapy				0.851
No/unknown	3725 (91.3%)	2609 (91.4%)	1116 (91.2%)	
Yes	353 (8.7%)	245 (8.6%)	108 (8.8%)	
Chemotherapy				0.427
No/unknown	2146 (52.6%)	1514 (53.0%)	632 (51.6%)	
Yes	1932 (47.4%)	1340 (47.0%)	592 (48.4%)	
Bone				0.367
No	4059 (99.5%)	2843 (99.6%)	1216 (99.3%)	
Yes	19 (0.5%)	11 (0.4%)	8 (0.7%)	
Brain				0.229
No	4046 (99.2%)	2828 (99.1%)	1218 (99.5%)	
Yes	32 (0.8%)	26 (0.9%)	6 (0.5%)	
Lung				0.800
No	3773 (92.5%)	2643 (92.6%)	1130 (92.3%)	
Yes	305 (7.5%)	211 (7.4%)	94 (7.7%)	
Liver				0.084
No	4014 (98.4%)	2816 (98.7%)	1198 (97.9%)	
Yes	64 (1.6%)	38 (1.3%)	26 (2.1%)	
Tumor size				0.538
Variable	**Total**	**Training**	**Validation**	***P*-value**
≤4	2074 (50.9%)	1461 (51.2%)	613 (50.1%)	
>4	2004 (49.1%)	1393 (48.8%)	611 (49.9%)	
LVI				0.416
Absent	2352 (57.7%)	1661 (58.2%)	691 (56.5%)	
Present	1282 (31.4%)	893 (31.3%)	389 (31.8%)	
Unknown	444 (10.9%)	300 (10.5%)	144 (11.8%)	
LDH				0.305
normal	3183 (78.1%)	2239 (78.5%)	944 (77.1%)	
<1.5	563 (13.8%)	396 (13.9%)	167 (13.6%)	
1.5–10	258 (6.3%)	167 (5.9%)	91 (7.4%)	
>10	74 (1.8%)	52 (1.8%)	22 (1.8%)	

SGCT, seminomatous germ cell tumor; nSGCT, non-seminomatous germ cell tumor; Mix-GCT, mixed germ cell tumor. LVI, lymph-vascular invasion.
[a] Statistical significance.

TGCTs (ICD: codes: 9061 to 9064, 9070 to 9071, 9080 to 9085, and 9100 to 9101), (3) TGCTs as the first primary tumor, and (4) adequate information on variables including demographic and clinicopathological. Exclusion criteria were the following: (1) Marital status unknown (n = 903), (2) Race unknown (n = 192), (3) Bilateral or unknown lateral (n = 167), (4) Tx/Nx (n = 487, n = 238), (5) Bone/brain/liver/lung metatasis unknown (n = 27. n = 2. n = 3. n = 15), (6) Tumor size unknown (n = 332), (7) Survival time less than one-month (n = 76) and (8) LDH unknown(n = 5941). In addition, patients who had an autopsy or died were ruled out from our study. After selection, 4078 eligible patients were enrolled in the cohort. In Fig. 1, we show how we selected the patients for this study.

2.2. Variables Defined

The variables in the selected cohort included: demographic characteristics (age at diagnosis, race, marital status), tumor characteristics (laterality, histologic type, the seventh AJCC edition T/N staging, distant metastatic site (bone, brain, liver), tumor size,

Table 2
Logistic regression analysis of independent risk factors of LM in TGCT patients.

Variable	Univariable analysis OR=(CI 95%)	*P*-value	Multivariate analysis OR=(CI 95%)	*P*-value
Marital				
Married	Ref		Ref	
Unmarried	3.355(2.377–4.853)	<0.001***	1.645(1.100–2.502)	0.017[a]
Age				
≤40	Ref			
>40	0.714(0.483–1.024)	0.077		
Race				
White	Ref			
Black	0.495(0.073–0.097)	0.237		
Other	0.522(0.245–0.976)	0.062		
Histology				
SGCT	Ref		Ref	
nSGCT	19.506(10.890–37.619)	<0.001***	9.211(4.837–1.867)	<0.001***
Mix-GCT	15.964(9.353–29.766)	<0.001***	8.555(4.820–1.644)	<0.001***
Lateral				
Left	Ref			
Right	0.856(0.646–1.133)	0.276		
T stage				
T1-T2	Ref		Ref	
T3-T4	7.084(4.866–10.210)	<0.001***	2.704(1.673–4.341)	<0.001***
N stage				
Node-negative	Ref		Ref	
Node-positive	6.393(4.760–8.656)	<0.001***	1.293(0.896–1.873)	0.171
Radiotherapy				
No/unknown	Ref			
Yes	0.865(0.491–1.421)	0.59		
Chemotherapy				
No/unknown	Ref		Ref	
Yes	54.824(25.050–154.471)	<0.001***	22.524(9.715–66.037)	<0.001***
Bone				
No	Ref		Ref	
Yes	22.638(6.780–87.024)	<0.001***	2.919(0.651–13.763)	0.159
Brain				
No	Ref		Ref	
Yes	169.476(49.834–1059.742)	<0.001***	44.837(10.737–329.230)	<0.001***
Liver				
No	Ref		Ref	
Yes	35.111(17.602–74.903)	<0.001***	6.396(2.697–16.032)	<0.001***
Tumor size				
≤4	Ref		Ref	
Variable	**Univariable analysis OR=(CI 95%)**	***P*-value**	**Multivariate analysis OR=(CI 95%)**	***P*-value**
>4	1.543(1.162–2.056)	0.0028**	1.050(0.733–1.505)	0.790
LVI				
Absent	Ref		Ref	
Present	3.193(2.344–4.376)	<0.001***	1.053(0.715–1.553)	0.793
Unknown	2.619(1.663–4.040)	<0.001***	1.464(0.836–2.514)	0.174
LDH				
normal	Ref		Ref	
<1.5	4.605(3.223–6.547)	<0.001***	2.587(1.712–3.891)	<0.001***
1.5–10	12.230(8.228–18.100)	<0.001***	3.667(2.239–5.964)	<0.001***
>10	12.777(6.378–23.456)	<0.001***	3.367(1.481–7.344)	0.003**

SGCT, seminomatous germ cell tumor; nSGCT, non-seminomatous germ cell tumor; Mix-GCT, mixed germ cell tumor. LVI, lymph-vascular invasion.
[a] Statistical significance.

lymphovascular invasion, postoperative serum LDH), and therapy information (radiotherapy, and chemotherapy). Some of the variables were regrouped in the analysis. We used the cutoff value of 40 years old in categorizing the covariate "age at diagnosis," which is described in the scientific literature as having prognostic significance [11,12]. Those patients in the SEER database whose marital status is "Divorced", "Single", "Unmarried" or "Widowed" have been regrouped into "Unmarried". The histology types were classified into SGCTs (code 9061–9063), NSGCTs (code 9070–9071,9080-9084,9100) and Mix-GCTs (code 9085,9101). The T stage was regrouped into T1-T2(localized disease) and T3-T4(locally advanced disease). The N stage was also regrouped into node-negative (N0) and node-positive (N1/N2/N3). According to the median and mean tumor size, the cut-off point was set at 4 cm.

2.3. Statistical analysis

Statistical analysis was performed in 3 steps. In the first step, based on a ratio of 7:3, we randomly divided the study population into training and validation cohorts. The Chi-square test and Mann-Whitney's *U* test were used to compare the baseline information for each group. In the second step, we performed a univariate logistic analysis to discern factors associated with lung metastasis. Variables with *P*-values less than 0.05 in univariate analysis were included in multivariate logistic regression to identify independent risk factors for lung metastases (LM) in testicular germ cell tumor (TGCT) patients. After that, the rms package in R software was used to create a predictive model for LM using independent factors in patients with TGCTs. In the third step, we plotted the ROC curve and computed the AUC to evaluate the diagnostic nomogram's discrimination. Likewise, compare the AUC of each independent risk factor to the AUC of the nomogram. Furthermore, the predictive nomogram was additionally evaluated by generating a calibration curve and performing a decision curve analysis (DCA). If the model is well-calibrated, the predictions should fall on the 45-degree diagonal. Statistical analyses were performed with SPSS 26 and R version 4.1.3. The significance level for all tests was set at 0.05 on a two-sided basis.

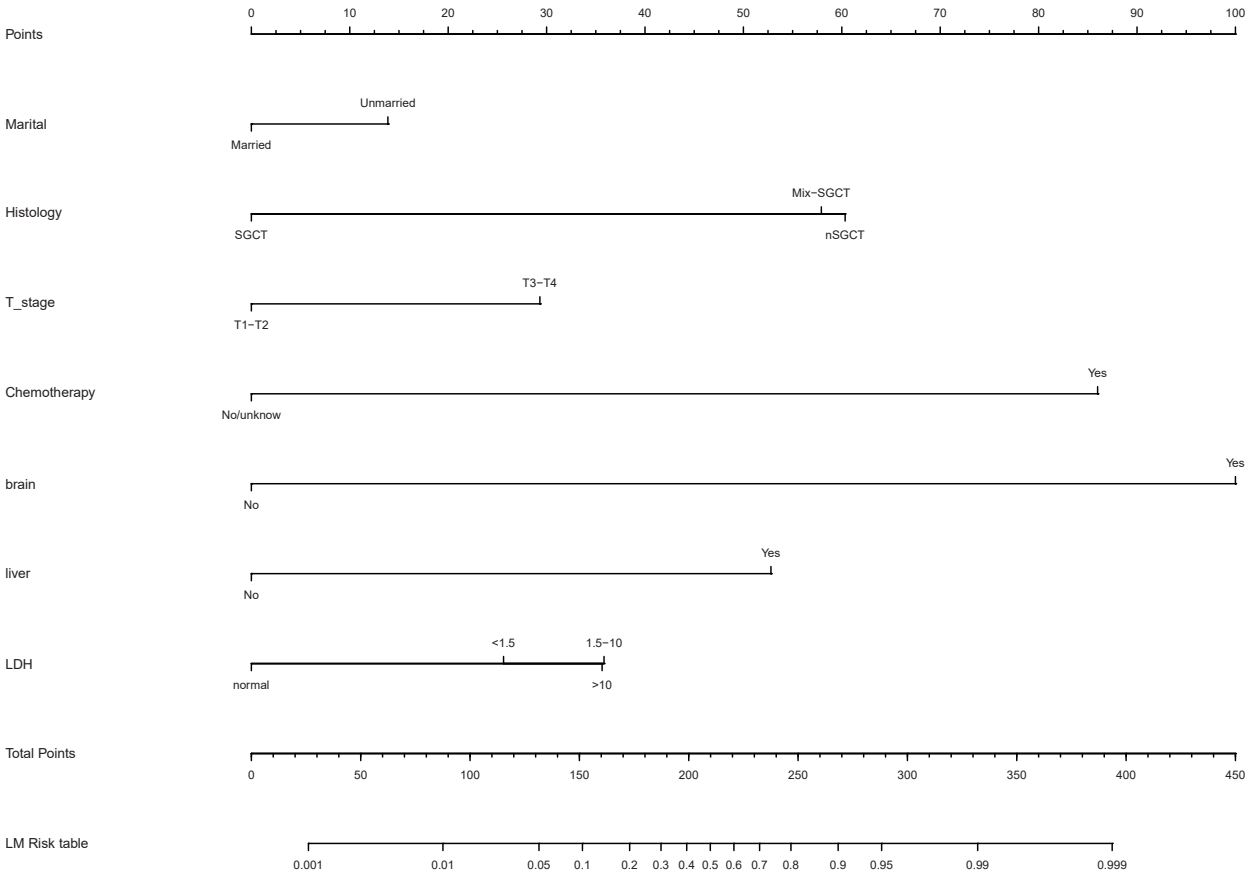

Fig. 2. Nomogram for lung metastasis of patients with TGCTs, use: locate patient values at each axis. Draw a vertical line to the "Point" axis to determine how many points are attributed for each variable value. Sum the points for all variables. Locate the sum on the "Total Points" line. Then, a vertical line is drawn from the total point scale to the LM axis to obtain the probability.

3. Results

3.1. Demographic and clinical characteristics

In Table 1, the demographics and clinical characteristics of the total cohort (n = 4078), training cohort (n = 2854), and validation cohort (n = 1224) are presented. All original data can be downloaded from the provided website (https://www.jianguoyun.com/p/DYrXAE8Ql_2ACxjn7JcFIAA). In the total cohort, 78% of the patients were younger than 40 years old, and 90% were white. Cancer characteristics and treatment: 1) the most common T stage and N stage, respectively, were T1-2 (94.2%) and N0 (73.4%), and 2) the proportion of patients with nonseminomas (NSGCTs) in this study was 12.8%, and 78.1% of the patients in this study had normal LDH levels, and 3) nineteen hundred thirty-two (47.4%) of the patients received chemotherapy and three hundred fifty-three (8.7%) patients received radiotherapy. No statistically significant differences were observed between the two groups of variables except for race. ($p < 0.05$).

3.2. Risk factors for lung metastasis (LM) in testicular germ cell tumors (TGCTs) patients

In the training cohort, the results of the univariate logistic regression analysis showed that marital status, tumor histological type, T/N stage, bone metastasis, brain metastasis, liver metastasis, tumor size, lymphovascular invasion, chemotherapy, and LDH are risk factors for testicular germ cell tumors lung metastasis. Subsequently, these variables were further incorporated into the multivariate analysis, which revealed that marital status, tumor histological type, T stage, brain metastasis, liver metastasis, LDH, and chemotherapy were independent predictors for LM in TGCT patients. Table 2 provides details.

3.3. Nomogram construction and validation

Combined with the univariate and multivariate logistic regression analysis, we constructed a nomogram to predict lung metastasis in patients with TGCTs (Fig. 2). Each variable in the nomogram was assigned a score ranging from 0 to 100, reflecting its respective contribution to the predictive model (Table 3). In Fig. 3A and B, the ROC curves show that the model is accurate and valid, with an AUC of 0.922 (95% CI, 0.907–0.936) in the training queue and 0.932 (95% CI, 0.910–0.951) in the validation queue. Results show that all calibration plots closely fall on a 45-degree diagonal line (Fig. 4A and B). DCA has proven to be clinically useful in training and validation queues (Fig. 5A and B). Additionally, the nomogram indicates a greater predictive accuracy than TN staging. Finally, as shown (Fig. 6A and B), the AUC for the combined nomogram is greater than the AUC for any of the independent predictors individually.

4. Discussion

Testicular cancer incidence rates are on the rise in many countries since the middle of the 20th century [13]. In 2019, there will be

Table 3
Nomogram scoring system.

Variables	Points	Variables	Points
Marital		LM probability	Total-points
Married	0	10%	151.40108
Unmarried	13.87301	20%	172.97768
Histology		30%	187.31835
SGCT	0	40%	199.07427
nSGCT	60.33822	50%	209.86244
Mix-GCT	57.92013	60%	220.65060
T stage		70%	232.40652
T1-T2	0	80%	246.74719
T3-T4	29.3187	90%	268.32380
Chemotherapy			
No/unknown	0		
Yes	85.99363		
Liver			
No	0		
Yes	52.79772		
Brain			
No	0		
Yes	100		
LDH			
normal	0		
<1.5	25.62627		
1.5–10	35.83679		
>10	35.64041		

SGCT, seminomatous germ cell tumor; nSGCT, non-seminomatous germ cell tumor; Mix-GCT, mixed germ cell tumor.

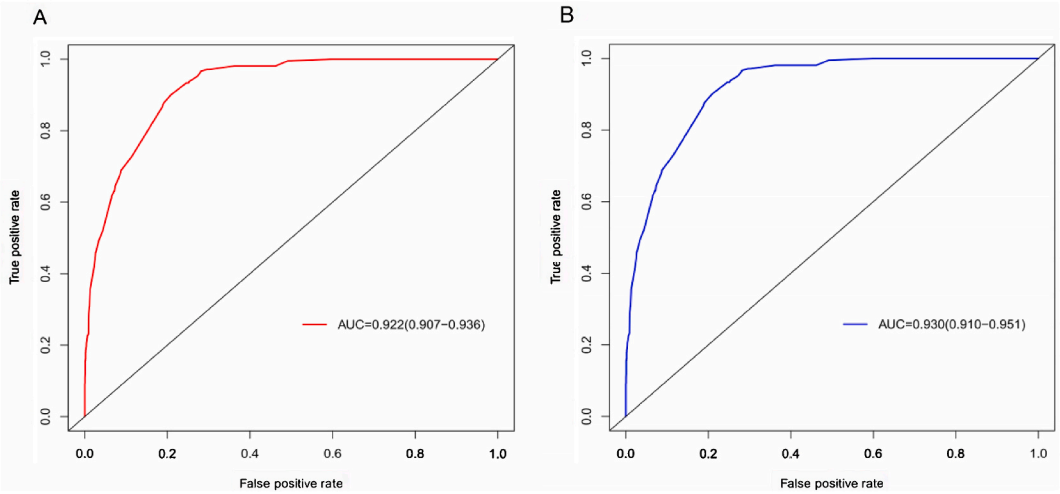

Fig. 3. The ROC of the nomogram of training cohort (A) and validation cohort (B).

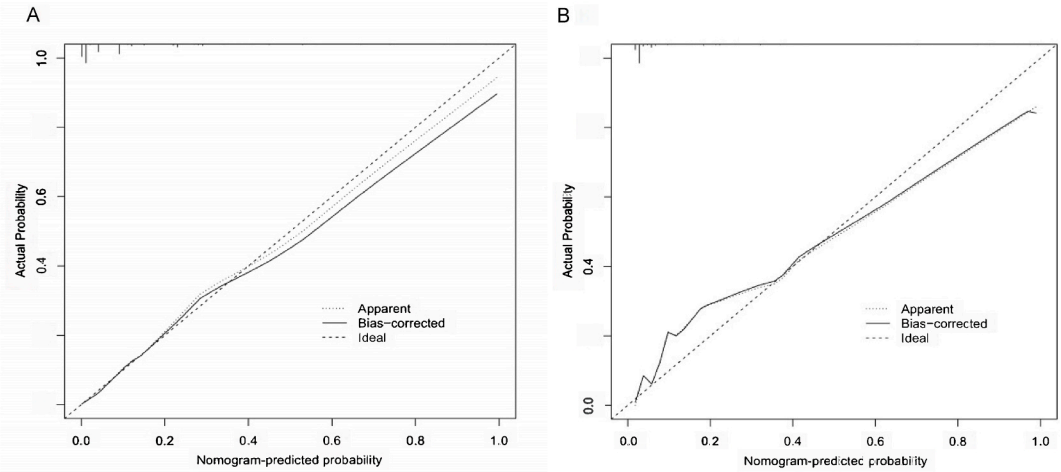

Fig. 4. The nomogram's calibration curve in the training cohort (A) and the validation cohort (B).

9560 new cases of testicular cancer in the United States, leading to 410 deaths [14]. Poor prognosis in patients with testicular germ cell tumors is driven primarily by the involvement of distant metastases [15]. The most common sites of metastatic testicular germ cell tumors include the lymph nodes and lungs. Interestingly, no studies have attempted to develop an ideal predictive model to predict the risk of lung metastases (LM) in testicular germ cell tumors (TGCTs), meaning it is impossible to quantify the likelihood of LM. Thus, using the largest cohort examined so far, we have developed an accurate nomogram to quantitatively predict the risk of LM in patients with TGCTs. Nomograms predict a specific outcome based on a combination of many important predictors, and they have become a practical clinical tool widely used in cancer research [16–18]. A score of 0–100 was assigned for each variable in the nomogram, and each patient received their total score by summing the scores in every subgroup. The higher the score, the greater the risk of developing lung metastases. First, metastasis in the brain was found to be the most important risk factor for LM metastasis of TGCTs. As reported in previous studies, brain metastases usually coexist with pulmonary metastases [7,19]. Feldman et al. [19] reported that brain metastases may be more common in patients with a high systemic disease burden, especially those with lung metastases. As lung metastases are more common in patients with brain metastases, a chest CT scan should be conducted in patients with respiratory symptoms. Similarly, for patients with pulmonary metastases, a head MRI should be performed when neurological symptoms are present. Thus, it is worthwhile to investigate whether other extrapulmonary metastases have synergistic effects on the development of LM. Additionally, we observed that liver metastasis is also a significant risk factor. According to previous reports [5], liver and bone metastases are associated with the poorest prognosis in metastatic TGCTs. Patients with liver metastases often represent a more aggressive tumor behavior that extends beyond the primary site, raising concerns about potential lung metastases. As a secondary outcome, we also found that the histological type of tumor was significantly related to lung metastasis. In patients with non-seminomatous germ cell tumors, the risk of lung metastasis is the highest, followed by mixed germ cell tumors, and seminomatous

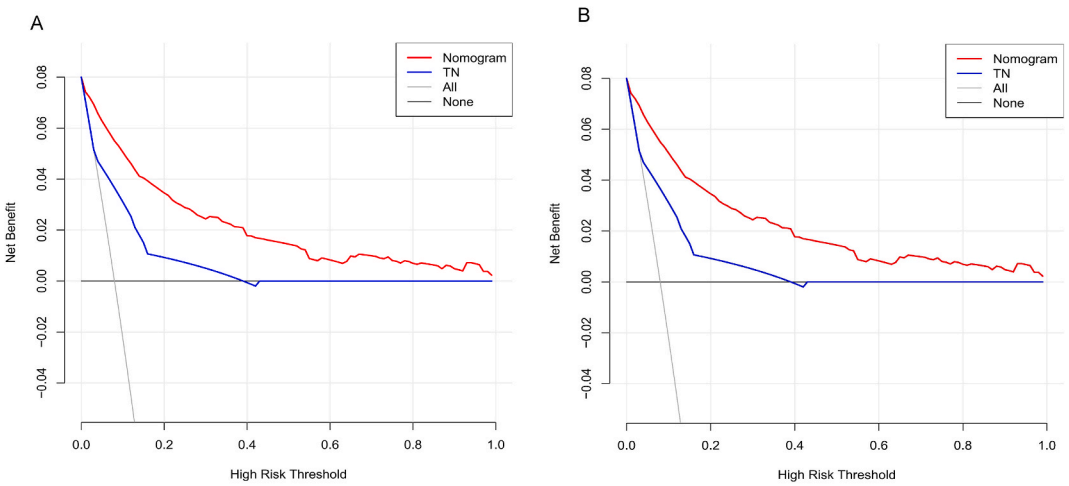

Fig. 5. (A) Decision curves of the nomogram predicting distant metastasis in the training cohort and (B) the validation cohort. The x-axis is the risk threshold, and the y-axis is the net benefit. The purple line indicates no distant metastasis of the patient, and the blue line shows that all patients have metastasis. When the threshold probability is between 0 and 100%, the net benefit of the model is the largest.

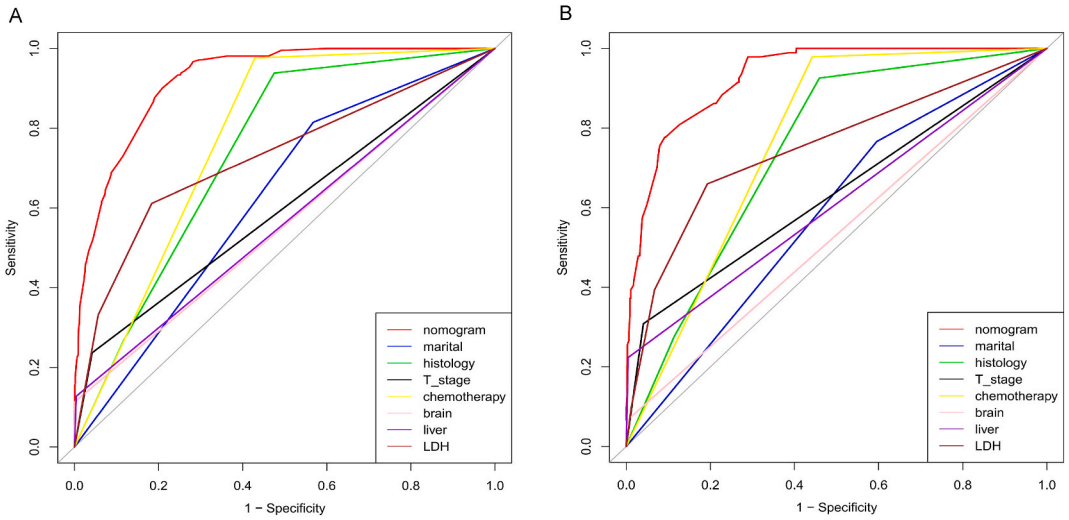

Fig. 6. Comparison of AUC between diagnostic nomogram and each independent predictor in the training cohort (A) and the validation cohort (B).

germ cell tumors have the lowest risk. The results that we obtained were similar to those of Akan et al. [20], who proposed that the risk of metastasis was higher in mixed germ cell tumors than in pure seminomatous germ cell tumors. In addition, the T stage is also a crucial factor for tumor metastasis. During our study, we found a greater risk of tumor metastasis with a higher T stage. This is logical since the tumor crosses blood vessels releases cancer cells into the bloodstream. Third, postoperative serum LDH is also a key factor for lung metastasis of tumors. Men with TGCTs have increased LDH levels in 40–60% of cases [21,22]. The level of serum LDH correlates with tumor burden and growth rate, as well as with cellular proliferation, and is typically higher in patients with advanced disease [23]. This means that LDH is also important for disease surveillance and follow-up for these patients. There are five LDH isoenzymes, and each LDH isoenzyme subunit contains either LDHA, LDHB, or both [24]. The LDH-1 tetramer consists of four LDHB subunits, whereas the LDH-5 tetramer consists of four LDHA subunits. Male adults have a specific LDH isoenzyme, LDH-X, that is a tetramer of four LDHC subunits* specific to testicular germ cells. All three LDH isoenzymes can be encoded by LDHA, LDHB, and LDHC. Eyben et al. [22] suggested that seminoma and non-seminomatous germ cell tumors have high RNA expression of LDHB. There are major biologic effects of LDHB. When LDHB is knocked down in lung carcinoma cells, cell growth is reduced. Likewise, knocking down LDHB also reduced the proliferation of cells in maxillary sinus cancer. All in all, other types of malignancies are also affected by LDHB [25].

In addition to the above findings, we identified several other significant risk factors. Fourth, patients with primary testicular tumors who have received chemotherapy are also considered at risk for lung metastasis. This is consistent with previous reports that patients undergoing chemotherapy or radiation therapy for testicular tumors are more prone to second tumor occurrences [26]. Lastly, an

interesting observation is that marital status, particularly among unmarried patients, is a predictive risk factor for lung metastasis. Ke et al. suggested that marital status could impact the prognosis of testicular tumor patients, potentially due to inadequate social support among unmarried patients, leading to less effective treatment [27]. However, we speculate that the lack of family support in unmarried patients' follow-up care might lead to delayed detection and diagnosis, potentially making distant metastasis more likely. Indeed, these findings warrant further exploration. The literature references for the risk factors presented in the nomogram can all be found in Table 4. From previous studies [5–7], three points can be drawn: among patients with metastasis, 1) the prognosis is worse than that of non-metastasizing patients, 2) the prognosis for patients with one metastasis is better than for those with multiple metastases, and 3) even if the distant metastases, early detection will help subsequent treatment and improve overall survival time. It is vital to diagnose lung metastases early in the course of treatment for testicular germ cell tumors since they are one of the most common metastatic sites for these tumors. For one thing, early diagnosis provides patients the chance for thoracic metastasectomy. For another, resection of pulmonary metastases has guiding significance for subsequent treatment, especially for further chemotherapy. The development process of our nomogram identified the following independent risk factors that can predict LM in TGCTs: marital status, histological type, T stage, brain metastatic status, liver metastatic status, chemotherapy, and LDH. We built a graph using these factors to predict lung metastasis. Additionally, patients achieving a cumulative score of 220 or higher on the nomogram should undergo intensified follow-up, as there is a 60% probability of lung metastasis occurrence. As a result of internal validation, the AUC of the diagnostic model was 0.930, and the calibration curve and DCA both delivered excellent results. What's more, according to the ROC analysis in our study, the nomogram had better discriminate power than any independent risk factor, again expounding the importance of an integrated predictive model. Our diagnostic model can provide a feasible, theoretical basis for clinical decisions and outpatient follow-up of patients. By better monitoring patients at high risk of lung metastasis, we can improve survival rates and quality of life for patients with testicular germ cell tumors. However, this study also had some limitations worth mentioning. Firstly, it is a retrospective study based on the public database (SEER). As well known, retrospective studies have several inherent problems such as selection bias and information bias, which cannot be ignored. Consequently, prospective clinical trials are necessary to test the prediction model's accuracy. Second, as a result of our screening process, we found that all patients included in the study had undergone surgery, so our diagnostic nomogram does not apply to those who did not. In the end, even though the validation cohort was internally validated, the results of this validation mean were not perfect since the patients developed and validated came from an identical database. Further external validation is therefore needed to confirm the accuracy and dependability of our nomogram.

5. Conclusion

In this study, our predict model revealed that marital status, tumor histological type, T stage, brain metastasis, liver metastasis, chemotherapy, and LDH were independent risk factors for lung metastasis patients with testicular germ cell tumors. All of these factors could be readily obtained in most hospitals, and the nomogram obtained good applicability. A more important finding was the development of a new accurate and visible nomogram that predicts the risk of lung metastases among patients with germ cell tumors of the testis. Doctors and patients can use this nomogram to monitor and identify lung metastasis of tumors through active monitoring and follow-up.

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Authors' contributions

Sheng Li: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Xiaoqiang Liu: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data. Jun Deng; Weipeng Liu; Fucun Zheng: Conceived and designed the experiments; Performed the experiments. Bin Fu: Conceived and designed the experiments; Wrote the paper. Situ Xiong; Jiahao Liu: Analyzed and interpreted the data; Wrote the paper. Wen Deng: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data. Lin Yang: Performed the experiments; Wrote the paper. Ming Jiang: Contributed reagents, materials, analysis tools or data; Wrote the

Table 4
The clinical significance of the variables is reported in other literature.

Variables in nomogram	Affected variable	Ref.
Marital	**prognosis**	[27]
Histology	**metastasis/prognosis**	[20]
T stage	**prognosis**	[28]
Chemotherapy	**progression**	[26]
Liver	**prognosis**	[5]
Brain	**metastasis**	[7,19]
LDH	**progression**	[23,24]

paper.

Data availability statement

All clinical information and data used for this study were available from public databases.

Ethics approval and consent to participate

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The SEER database provides clinical data about cancer patients, which greatly facilitates clinical research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20177.

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