Development, validation, and visualization of a web-based nomogram for predicting the incidence of leiomyosarcoma patients with distant metastasis

Zhehong Li | Junqiang Wei | Haiying Cao | Mingze Song | Yafang Zhang | Yu Jin

Abstract

Background: Leiomyosarcoma (LMS) is one of the most common soft tissue sarcomas. LMS is prone to distant metastasis (DM), and patients with DM have a poor prognosis. Aim: In this study, we investigated the risk factors of DM in LMS patients and the prognostic factors of LMS patients with DM. Methods and results: LMS patients diagnosed between 2010 and 2016 were extracted from the Surveillance, Epidemiology, and End Result (SEER) database. Patients were randomly divided into the training set and validation set. Univariate and multivariate logistic regression analyses were performed, and a nomogram was established. The area under the curve (AUC), calibration curve, and decision curve analysis (DCA) were used to evaluate the nomogram. Based on the nomogram, a web-based nomogram is established. The univariate and multivariate Cox regression analyses were used to assess the prognostic risk factors of LMS patients with DM. Eventually, 2184 patients diagnosed with LMS were enrolled, randomly divided into the training set (n = 1532, 70.14%) and validation set (n = 652, 29.86%). Race, primary site, grade, T stage, and tumor size were correlated with DM incidence in LMS patients. The AUC of the nomogram is 0.715 in training and 0.713 in the validation set. The calibration curve and DCA results showed that the nomogram performed well in predicting the DM risk. A web-based nomogram was established to predict DM’s risk in LMS patients (https://wenn23.shinyapps.io/riskoflmsdm/). Epithelioid LMS, in uterus, older age, giant tumor, multiple organ metastasis, without surgery, and chemotherapy had a poor prognosis.

Conclusions: The established web-based nomogram (https://wenn23.shinyapps.io/riskoflmsdm/) is an accurate and personalized tool to predict the risks of LMS developing DM. Advanced age, larger tumor, multiple organ metastasis, epithelioid type, uterine LMS, no surgery, and no chemotherapy were associated with poor prognosis in LMS patients with DM.
1 | INTRODUCTION

Leiomyosarcoma (LMS) is one of the most common soft tissue sarcomas, accounting for 12% of all soft tissue sarcomas.\(^1\) It is reported that LMS mainly occurs in 50–60 years old patients and is often involved in the uterus, retroperitoneal space, and soft tissue.\(^2\) About 25% of LMS patients will occur DM even through radical resection.\(^3,4\) Okamoto et al. have reported that the common metastatic sites of LMS include lung, liver, and bone.\(^5\) Further studies have shown that lung is the most common metastatic site.\(^3,5\) Some studies have demonstrated that the survival rate of LMS patients is improving after receiving chemotherapy and surgery. However, the prognosis of LMS patients with DM is still poor, and the 5-year survival rate was less than 20%.\(^5–8\) Leiomyosarcoma accounts for about 0.12% of all tumors, and because of the low incidence rate of LMS, the risk factors, and prognostic factors of DM are not yet clear.\(^1\) Therefore, identifying high-risk LMS patients who are at risk of developing DM is meaningful. Many studies have shown that malignant tumor prognosis can be more accurate, more effective, and more beneficial by using nomograms.\(^9,10\) Takehara et al. have analyzed the clinical status and prognosis of uterine LMS patients.\(^6\) Xue et al. have investigated the prognosis of extremities LMS patients and established a prognostic nomogram.\(^11\) However, as far as we know, there is no research on building a web-based nomogram to estimate the DM risk in LMS patients. Besides that, there are no studies to predict the prognosis of LMS with DM. Therefore, we intend to use the Surveillance, Epidemiology, and End Results (SEER) database to evaluate DM incidence and risk factors in LMS and establish a visualized web-based nomogram.\(^12\) Furthermore, we intend to predict the prognostic factors of LMS patients with DM.

2 | MATERIALS AND METHODS

2.1 | Patients

The data included in the present study were downloaded from the SEER\(^*\)Stat software version 8.3.6.\(^12\) Using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3), we identified all LMS patients (ICD-O-3 histologic type: 8890, 8891, 8893, 8896). We collected case diagnosis time between 2010 and 2016. The inclusive criteria were as follows: (1) patients with pathological diagnosis of LMS, (2) patients from the time of 2010–2016, according to the term “year of diagnosis,” (3) complete follow-up information, no data loss. The exclusion criteria were as follows: (1) patients missing essential details, including grade, stage, tumor size, surgery, radiotherapy, chemotherapy, survival time, and marital status, (2) follow-up status is missing. According to the ethics guidelines, neither informed consent nor approval of the ethics committee is required because we use public and anonymous data.

2.2 | Data element

The following demographic and clinical characteristics were included: age, sex (Female and Male), race [white, black, and others (American Indian/AK Native, Asian/Pacific Islander)], marital status (married and unmarried), grade (I–II or III–IV), T stage (I–II or III–IV), N stage (N0 or N1), surgical treatment (No or Yes), radiation treatment (No or Yes), chemotherapy (No or Yes), tumor size, and the histologic type (LMS NOS, Epithelioid LMS, Bizare LMS, and Myxoid LMS). The primary site was divided into uterus, soft tissue, retroperitoneum, others (eye and orbit, bones and joints, other digestive organs, trachea mediastinum, and other respiratory organs), distant metastasis (DM; No metastasis, oligo metastasis, and multiple metastases). The survival analysis’s primary outcome was the overall survival (OS), defined as the time from diagnosis to death due to any cause.

2.3 | Statistical analysis

The eligible patients were randomly divided into training set (n = 2184, 70%) and testing set (n = 652, 30%). In this study, patients in the training set were used to establish a nomogram, and patients in the test group were used to verify the nomogram. In this study, p-value <.05 (bilateral) was considered statistically significant. Univariate and multivariate logistic regression models were used to analyze the risk factors of DM in LMS patients. Based on these independent risk factors, a nomogram was established by R software. The nomogram was then evaluated by receiver operating characteristic curve (ROC), calibration curve analysis, and decision curve analysis (DCA). A web-based nomogram was further prepared based on the nomogram by the “Dynom” package. The survival time was measured by the Kaplan–Meier analyzes, and the difference between DM and without DM was tested by log-rank test. Cox proportional hazard regression model was used for univariate and multivariate analysis, and significant variables were obtained. All statistical analyses were performed using R software (http://www.Rproject.org, version 4.0.3).

3 | RESULTS

3.1 | Demographic and clinical characteristics

A detailed workflow was shown in Figure 1. According to the predetermined criteria, a total of 2184 LMS patients were included. There
were 699 males (32.01%) and 1485 females (67.99%). As for race, most of the patients were White (n = 1677 [76.33%]), followed by Black (n = 324 [14.84%]) and Others (n = 193 [8.84%]). The most common site of primary tumor is soft tissue (n = 1176 [53.85%]), followed by uterus (n = 668 [30.59%]), retroperitoneal (n = 300 [13.74%]), and others (n = 40 [1.83%]). The most common histological type was LMS NOS (n = 2103 [96.29%]), the others (Epithelioid LMS, Bizare LMS, and Myxoid LMS) were 81 cases (3.71%). Differentiation in grades III–IV (n = 1434, 65.66%) was the most common among tumor classifications. T1–2 (n = 2068, 94.69%) and N0 (n = 2098, 6.68%) phases were common. Of all the patients, 1185 (86.31%) had no metastasis, 222 (10.16%) had oligo metastasis and 77 (3.53%) had multiple metastases. Treatment methods selected by LMS patients included surgery (n = 1995 [91.35%]), chemotherapy (n = 1489 [68.18%]), and radiotherapy (n = 1467 [67.17%]). More details are shown in Table 1.

### 3.2 Risk factors for DM development in LMS patients

An odds ratio (OR) greater than 1 indicates that the exposure is a risk factor, a OR less than 1 indicates a protective factor, and a value equal to 1 indicates an unrelated factor. Age, sex, race, grade, T stage, N stage, site, size, and histologic type were related to DM developing DM in univariate logistics analysis. In multivariate logistics analysis, the Black (OR = 1.445, 95% CI = 1.039–2.008, p-value = .028), grade III–IV (OR = 2.873, 95% CI = 2.030–4.067, p-value < .001), N1 stage (OR = 3.428, 95% CI = 2.125–5.532, p-value < .001), primary site in uterus (OR = 1.754, 95% CI = 1.239–2.483, p-value = .002) and tumor size (OR = 1.002, 95% CI = 1.001–1.004, p-value < .001) were risk factors for DM in LMS patients. More details are shown in Table 2 and Figure 2.

### 3.3 Diagnostic nomogram development and validation

We constructed a nomogram according to the logistics regression analysis results, including all risk factors for DM in LMS patients (Figure 3). The area under the curve (AUC) of the nomogram is 0.715 in the training and 0.713 in the validation set (Figure 4). The calibration curve shows a high degree of agreement between the nomogram’s predicted results and the desired results in the training set (Chi-square = 5.236, p-value = .813, Figure 5A) and the validation set (Chi-square = 7.171, p-value = .619, Figure 5B). Besides, DCA shows that the nomogram can be used as an excellent model to infer the risk of LMS with DM in the training set (Figure 6A) and the validation set (Figure 6B).

### 3.4 The web-based nomogram

A web version ([https://wenn23.shinyapps.io/riskoflmsdm/](https://wenn23.shinyapps.io/riskoflmsdm/)) was constructed. On the left side of the page are our extrapolated risk factors for DM. According to the patient’s condition, clinicians can select the corresponding features in the left interface. Click on the “predict” button, and the right screen shows the prediction of the patient’s risk of DM and the specific 95% confidence interval. To help others better understand the operation process of a web-based nomogram, we randomly enumerate four virtual cases in Figure 7. The four different
| Subject characteristics | Total cohort | Training cohort | Validation cohort |
|-------------------------|-------------|----------------|------------------|
| Age                     |             |                |                  |
| Median (range, years)   | 61 (1–101)  | 61 (2–97)      | 60 (6–101)       |
| Sex                     |             |                |                  |
| Male                    | 699         | 489            | 210              |
| Female                  | 1485        | 1043           | 442              |
| Race                    |             |                |                  |
| White                   | 1667        | 1174           | 493              |
| Black                   | 324         | 227            | 97               |
| Others                  | 193         | 131            | 62               |
| Marital status          |             |                |                  |
| Married                 | 1746        | 1217           | 529              |
| Unmarried               | 438         | 315            | 123              |
| Primary site            |             |                |                  |
| Soft tissue             | 1176        | 835            | 341              |
| Retroperitoneum         | 300         | 204            | 96               |
| Uterus                  | 668         | 467            | 201              |
| Others                  | 40          | 26             | 14               |
| Histologic type         |             |                |                  |
| LMS NOS                 | 2103        | 1483           | 620              |
| Epithelioid             | 51          | 28             | 18               |
| Bizarre                 | 2           | 1              | 1                |
| Myxoid                  | 28          | 20             | 8                |
| Grade                   |             |                |                  |
| I–II                    | 750         | 534            | 216              |
| III–IV                  | 1434        | 998            | 436              |
| T stage                 |             |                |                  |
| T1–T2                   | 2068        | 1455           | 613              |
| T3–T4                   | 116         | 77             | 39               |
| N stage                 |             |                |                  |
| N0                      | 2098        | 1469           | 629              |
| N1                      | 86          | 63             | 23               |
| Number of metastasis    |             |                |                  |
| 0                       | 1885        | 1309           | 576              |
| 1                       | 222         | 162            | 60               |
| >1                      | 77          | 61             | 16               |
| Tumor size              |             |                |                  |
| Median (range, mm)      | 85 (1–989)  | 85 (1–989)     | 85 (1–989)       |
| Surgery                 |             |                |                  |
| Yes                     | 189         | 142            | 47               |
| No                      | 1995        | 1390           | 605              |
| Radiotherapy            |             |                |                  |
| Yes                     | 717         | 500            | 217              |
| No                      | 1467        | 1032           | 435              |
**TABLE 1**  (Continued)

| Subject characteristics | Total cohort | | Training cohort | | Validation cohort | |
|--------------------------|--------------|---|-----------------|---|-----------------|---|
|                          | n            | %  | n              | %  | n              | %  |
| **Chemotherapy**         |              |    |                |    |                |    |
| Yes                      | 695          | 31.82 | 478            | 31.20 | 217            | 33.28 |
| No                       | 1489         | 68.18 | 1054           | 68.80 | 435            | 66.72 |
| **Vital status**         |              |    |                |    |                |    |
| Alive                    | 1258         | 57.60 | 877            | 57.25 | 381            | 58.44 |
| Dead                     | 926          | 42.40 | 655            | 42.75 | 271            | 41.56 |

**TABLE 2**  Logistic regression model for analyzing the risk factors for developing distant metastases in patients diagnosed with LMS

|                          | Univariate | | Multivariate | |
|--------------------------|------------|---|--------------|---|
|                          | OR         | 95%CI | P-value | OR | 95%CI | P-value |
| **Age**                  |            |      |         |    |      |         |
| Range (years)            | 0.991      | 0.983–0.999 | .034 | 0.996 | 0.986–1.005 | .349 |
| **Sex**                  |            |      |         |    |      |         |
| Male                     | Reference  |      |         |    |      |         |
| Female                   | 1.449      | 1.098–1.912 | .009 | 0.859 | 0.609–1.211 | .386 |
| **Race**                 |            |      |         |    |      |         |
| White                    | Reference  |      |         |    |      |         |
| Black                    | 1.627      | 1.188–2.227 | .002 | 1.445 | 1.039–2.008 | .028 |
| Others                   | 1.291      | 0.852–1.956 | .228 | 1.234 | 0.803–1.898 | .338 |
| **Primary site**         |            |      |         |    |      |         |
| Soft tissue              | Reference  |      |         |    |      |         |
| Retroperitoneum          | 1.152      | 0.772–1.717 | .489 | 1.033 | 0.683–1.562 | .879 |
| Uterus                   | 2.312      | 1.774–3.013 | <.001 | 1.754 | 1.239–2.483 | .002 |
| Others                   | 0.707      | 0.215–2.327 | .568 | 0.662 | 0.197–2.229 | .506 |
| **Histologic type**      |            |      |         |    |      |         |
| LMS NOS                  | Reference  |      |         |    |      |         |
| Epithelioid              | 1.971      | 1.020–3.809 | .044 | 1.23 | 0.615–2.460 | .559 |
| Bizarre                  | 0          | 0     | .999    | 0  | 0     | .999    |
| Myxoid                   | 0.769      | 0.231–2.562 | .668 | 0.661 | 0.191–2.287 | .514 |
| **Grade**                |            |      |         |    |      |         |
| I–II                     | Reference  |      |         |    |      |         |
| III–IV                   | 3.573      | 2.553–5.001 | <.001 | 2.873 | 2.030–4.067 | <.001 |
| **T stage**              |            |      |         |    |      |         |
| T1–2                     | Reference  |      |         |    |      |         |
| T3–4                     | 2.333      | 1.51–3.604 | <.001 | 1.001 | 0.614–1.634 | .995 |
| **N stage**              |            |      |         |    |      |         |
| N0                       | Reference  |      |         |    |      |         |
| N1                       | 4.064      | 2.576–6.410 | <.001 | 3.428 | 2.125–5.532 | <.001 |
| **Size**                 |            |      |         |    |      |         |
| Range (mm)               | 1.003      | 1.002–1.004 | <.001 | 1.002 | 1.001–1.001 | <.001 |
colored curves in part B represent the risk of DM and the 95% CI for different virtual cases. Part C reflects the specific values.

### 3.5 Survival outcome and prognostic factors for LMS patients with DM

A hazard ratio (HR) less than 1 indicates a protective effect; a HR greater than 1 indicates a detrimental effect. Univariate Cox analysis showed that age, tumor size, number of metastases, histological type, surgery, and chemotherapy were associated with OS. In multivariate Cox analysis, only age (HR = 1.012, 95% CI = 1.001–1.022, p-value = .026), tumor size (mm) (HR = 1.004, 95% CI = 1.002–1.006, p-value < .001), Epithelioid LMS (HR = 2.369, 95% CI = 1.304–4.306, p-value = .005), multiple metastases (HR = 1.48, 95% CI = 1.246–2.195, p-value < .001), surgery performed (HR = 1.895, 95% CI = 1.404–2.558, p-value < .001), and chemotherapy performed (HR = 1.654, 95% CI = 1.246–2.195, p-value < .001) were independent prognostic indicators of OS. More details are listed in Table 3.

### 3.6 Survival outcome for patients with DM

For patients without metastases, the 1-, 2-, and 3-year survival rates were 86.5%, 74.2%, and 65.1%, respectively. The median OS was 71 months. However, for metastatic patients, the 1-, 2-, and 3-year survival rates were 58.5%, 34.3%, and 20.6% with a median OS of 16.0 (95% CI: 13.622–18.378) months. The trend of OS for LMS patients with or without initial DM is illustrated in Figure 2.
LMS is an aggressive tumor of soft tissue sarcoma, and about 30% of LMS patients are prone to metastasize to distant organs. Existing evidence indicated that the median survival time of LMS patients with lung metastasis is 15 months. Therefore, it is crucial to identify the risk factors of LMS patients developing DM. At the same time, early intervention should be carried out for patients prone to DM to prolong the survival period. However, few studies have explored the risk of DM in LMS patients, and there was no relevant research on the web-based nomogram. Unlike previous nomograms, visualized web-based nomograms can accurately predict the risk of DM. The clinician can select the corresponding variable on the left side of the page according to the conditions of different patients to obtain the risk of patients with DM (Figure 7). It is an effective tool for developing personalized follow-up plans and providing health counseling. Therefore, we first established the web-based nomogram about the risk of DM in LMS patients based on the SEER database.

Previous studies have shown that grade is considered the most important prognostic factor of LMS and is also a predictive index of DM. In our study, we also found that high-grade LMS patients were more likely to develop DM. Additionally, it is worth noting that although lymph node (LN) metastasis is rare in LMS patients (n = 86, 3.94%), once LN occurs, it indicates that patients have a higher probability for DM (OR = 3.428, 95% CI = 2.125–5.532, p-value < .001). This observation was consistent with previous studies. A retrospective study has also shown that uterus LMS patients have a worse prognosis than non-uterine. In Lamm's opinion, compared with the retroperitoneal and extremity LMS, the uterus LMS is associated with a worse prognosis owing to late detection and negative clinical features. In contrast to Lamm's prediction, we further classified non-uterine tissues into soft tissues, retroperitoneum, and others. Our study showed that the prognosis of primary uterine LMS was the worst (OR = 1.754, 95% CI = 1.239–2.483, p-value = .002), and the prognosis of retroperitoneal LMS was similar to that of soft tissue LMS (OR = 1.033, 95% CI = 0.683–1.562, p-value = .879). Because LMS in other sites is rare (n = 40, 1.83%), it is not enough to infer
clinically significant results. Compared with Lamm’s research, we use the web-based nomogram to visually evaluate the prognosis of LMS patients with different characteristics and predict the risk of DM. Accumulating evidence demonstrated that early surgery and a negative surgical margin greatly reduce the potential of local recurrence and DM.\textsuperscript{20--22} Therefore, surgery is considered to be an

![Decision curve analysis](image1.png)

**FIGURE 6** Decision curve analysis of the nomogram for estimating the risk of LMS with DM in the training cohort (A) and validation cohort (B), respectively.

![Operation interface](image2.png)

**FIGURE 7** The operation interface of the nomogram on the web page. After entering a patient’s Race, Site, Grade, N stage, and Size on [https://wenn23.shinyapps.io/riskoflmsdm/](https://wenn23.shinyapps.io/riskoflmsdm/), the clinicians can get the LMS patient’s corresponding probability of developing DM. (A) Input interface, you can enter a patient’s Race, Site, Grade, N stage, and Size in this interface. (B) Graphical summary represents LMS patients’ corresponding probability and 95% confidence intervals of developing DM. (C) Numerical summary shows the actual values of probability and 95% confidence intervals.
important factor in the prognosis of patients. In addition, it should be noted that advanced age is associated with tumor metastasis and leads to a poor prognosis. Therefore, we hypothesized that this poor prognosis and higher DM risk were associated with poor physical function in older patients, who often suffer from chronic diseases. The benefit of chemotherapy on the survival of LMS patients is

### TABLE 3

|                | Univariate |          |          |          |          |          |          |
|----------------|------------|----------|----------|----------|----------|----------|----------|
|                | HR         | 95% CI   | P-value  | HR       | 95% CI   | P-value  |          |
| **Age**        | 1.012      | 1.002–1.023 | .017     | 1.012    | 1.001–1.022 | .026     |          |
| **Sex**        |            |          |          |          |          |          |          |
| Male           | Reference  |          |          |          |          |          |          |
| Female         | 1.165      | 0.864–1.571 | .318     |          |          |          |          |
| **Race**       |            |          |          |          |          |          |          |
| White          | Reference  |          |          |          |          |          |          |
| Black          | 0.997      | 0.721–1.380 | .986     |          |          |          |          |
| Others         | 0.862      | 0.556–1.336 | .057     |          |          |          |          |
| **Primary site** |          |          |          |          |          |          |          |
| Soft tissue    | Reference  |          |          |          |          |          |          |
| Retroperitoneum| 0.938      | 0.617–1.428 | .764     |          |          |          |          |
| Uterus         | 1.233      | 0.934–1.628 | .139     |          |          |          |          |
| Others         | 1.344      | 0.330–5.472 | .68      |          |          |          |          |
| **Histologic type** |        |          |          |          |          |          |          |
| LMS NOS        | Reference  |          |          |          |          |          |          |
| Epithelioid    | 1.852      | 1.003–3.318 | .038     | 2.369    | 1.304–4.306 | .005     |          |
| Myxoid         | 0.702      | 0.174–2.829 | .619     | 0.605    | 0.149–2.466 | .483     |          |
| **Grade**      |            |          |          |          |          |          |          |
| I–II           | Reference  |          |          |          |          |          |          |
| III–IV         | 1.385      | 0.938–2.045 | .102     |          |          |          |          |
| **T stage**    |            |          |          |          |          |          |          |
| T1–T2          | Reference  |          |          |          |          |          |          |
| T3–T4          | 2.108      | 1.401–3.171 | <.001    | 2.895    | 1.861–4.506 | <.001    |          |
| **N stage**    |            |          |          |          |          |          |          |
| N0             | Reference  |          |          |          |          |          |          |
| N1             | 1.112      | 0.743–1.664 | .606     |          |          |          |          |
| **Radiotherapy** |          |          |          |          |          |          |          |
| Yes            | Reference  |          |          |          |          |          |          |
| No             | 1.058      | 0.788–1.422 | .706     |          |          |          |          |
| **Chemotherapy** |          |          |          |          |          |          |          |
| Yes            | Reference  |          |          |          |          |          |          |
| No             | 1.36       | 1.040–1.777 | .025     | 1.654    | 1.246–2.195 | <.001    |          |
| **Number of mets** |        |          |          |          |          |          |          |
| 1              | Reference  |          |          |          |          |          |          |
| ≥2             | 1.735      | 1.298–2.319 | <.001    | 1.48     | 1.089–2.012 | .012     |          |
| **Marital status** |        |          |          |          |          |          |          |
| Yes            | Reference  |          |          |          |          |          |          |
| No             | 0.742      | 0.546–1.009 | .057     |          |          |          |          |
| **Surgery**    |            |          |          |          |          |          |          |
| Yes            | Reference  |          |          |          |          |          |          |
| No             | 1.813      | 1.376–2.390 | <.001    | 1.895    | 1.404–2.558 | <.001    |          |
| **Size**       |            |          |          |          |          |          |          |
|                | 1.004      | 1.002–1.006 | <.001    | 1.004    | 1.002–1.006 | <.001    |          |
controversial. Accumulating researches have shown that chemotherapy is an important factor in improving the prognosis of patients.\textsuperscript{23,24} However, other research concluded that adjuvant chemotherapy is not associated with significant survival benefits.\textsuperscript{25,26} Our findings support that chemotherapy improves the prognosis of LMS patients with DM. Besides that, LMS patients with multiple metastases were worse than those with oligo metastasis. Multiple metastases are closely related to the imbalance of multiple organ functions and the decline of patients’ quality of life.\textsuperscript{27} The present study had some limitations. First of all, the design of this study is a retrospective study, and selection bias is inevitable. Secondly, because the SEER database does not provide the exact surgical method, surgical margin distance, specific methods of chemotherapy and radiotherapy, and the severity of DM, we cannot get the impact of the above dates on LMS patient’s survival. The third limitation is that the order of treatment is not considered. Since the data set does not record relapse or progression, we must consider a baseline variable rather than a time-variant variable. We hypothesized that the exact combination of treatments was determined at the time of diagnosis. This assumption is necessary to integrate treatment information into the model in the absence of precise treatment timing. The fourth limitation is that the study only uses internal verification methods to verify the clinical application value of nomograms and lacks external verification. This shortcoming is also what our research group needs to improve in the next step. Finally, we included only patients diagnosed with LMS from 2010 to 2016, a more extensive time range and larger sample size may help to improve the reliability and persuasiveness of prediction further.

Despite the limitations of this study, the advantages of this study are as follows. First of all, the specific study methods and statistics involved in the nomogram were used to synthesize the baseline characteristics of patients with LMS. Results from this analysis can be used to predict DM in LMS patients. Secondly, in our study, the nomogram showed excellent performance in DM risk assessment, which will enable more accurate personalized clinical decision making and monitoring. Thirdly, to the best of our knowledge, our study is the first to focus on predicting the risk of DM for LMS patients. The results can be used as a basis for personalized treatment. Finally, the web-based nomogram is performed based on the nomogram, which has a friendlier window than the conventional nomogram and provides a more convenient and intuitive forecast probability.

5 | CONCLUSIONS

In conclusion, training and validation of the nomogram based on prognostic factors can provide satisfactory predictive efficiency. To encourage widespread clinical use, we developed a web-based nomogram (https://wenn23.shinyapps.io/riskoflmsdm/). It is an auxiliary graphical tool to evaluate the risks of DM in LMS patients. Advance age, epithelioid histologic type, larger tumor size, multiple metastases, no chemotherapy performed, and no surgery performed associated with worse survival in LMS patients with DM.

ACKNOWLEDGMENTS

We are very grateful for the contributions of the SEER database and the 18 registration agencies that provide information on cancer research, and colleagues involved in the study.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, Methodology, Software, Data Curation, Visualization, Formal analysis, and Writing - Original Draft, Z.L.; Conceptualization, Methodology, Data Curation, Writing - Original Draft, and Writing - Review & Editing, J.W.; Validation, Formal analysis, Data Curation, and Writing - Original Draft, H.C.; Data Curation, Validation and Formal analysis, M.S.; Data Curation, Validation and Formal analysis, Y.Z.; Writing - Review & Editing, Supervision, and Project administration, Y.J.

ETHICS STATEMENT

We have obtained permission to access research data files in the SEER program of the National Cancer Institute (reference number 18284-Nov2019). No ethical review is required because SEER data is publicly available and has been de-identified.

DATA AVAILABILITY STATEMENT

The data used in this study are freely accessible and can be obtained via the National Cancer Institute SEER database.

ORCID

Zhehong Li https://orcid.org/0000-0001-9385-0618
Junqiang Wei https://orcid.org/0000-0002-5196-821X
Yu Jin https://orcid.org/0000-0002-7101-8924

REFERENCES

1. Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: an update on the current state of histotype-specific management in an era of personalized medicine. CA Cancer J Clin. 2020;70(3):200-229. doi:10.3322/caac.21605
2. Farid M, Ong WS, Tan MH, et al. The influence of primary site on outcomes in leiomyosarcoma: a review of clinicopathologic differences between uterine and extraterine disease. Am J Clin Oncol. 2013;36(4):368-374. doi:10.1097/COC.0b013e3182488db4
3. Brennan MF, Antonescu CR, Moraco N, Singer S. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. Ann Surg. 2014;260(3):416-421. doi:10.1097/SLA.0000000000000869
4. Barone A, Chi DC, Theoret MR, et al. FDA approval summary: Trabectedin for unrespectable or metastatic liposarcoma or Leiomyosarcoma following an anthracycline-containing regimen. Clin Cancer Res. 2017;23(24):7448-7453. doi:10.1158/1078-0432.CCR-17-0898
5. Okamoto M, Matsuoka M, Soma T, et al. Metastases of soft tissue sarcoma to the liver: a historical cohort study from a hospital-based cancer registry. Cancer Med. 2020;9(17):6159-6165. doi:10.1002/cam4.3304
6. Takehara K, Yamashita N, Watanabe R, et al. Clinical status and prognostic factors in Japanese patients with uterine leiomyosarcoma. Gynecol Oncol. 2020;157(1):115-120. doi:10.1016/j.ygyno.2020.01.022
7. Qian SJ, Wu JQ, Wang Z, Zhang B. Surgery plus chemotherapy improves survival of patients with extremity soft tissue...
leiomyosarcoma and metastasis at presentation. J Cancer. 2019; 10(10):2169-2175. doi:10.7150/jca.29874
8. Kapp DS, Shin JY, Chan JK. Prognostic factors and survival in 1396 patients with uterine leiomyosarcomas: emphasis on impact of lymphadenectomy and oophorectomy. Cancer. 2008;112(4):820-830. doi:10.1002/cncr.23245
9. Mocellin S, Nitti D. Gastrointestinal carcinoid: epidemiological and survival evidence from a large population-based study (n = 25 531). Ann Oncol. 2013;24(12):3040-3044. doi:10.1093/annonc/mdt377
10. Callegaro D, Miceli R, Mariani L, Raut CP, Gronchi A. Soft tissue sarcoma nomograms and their incorporation into practice. Cancer. 2017; 123(15):2802-2820. doi:10.1002/cncr.30721
11. MingFeng X, Gang C, JiaPing D, et al. Development and validation of a prognostic nomogram for Extrki, Yoshida Yoshio. Molecular biomarkers for uterine leiomyosarcoma and endometrial stromal sarcoma. Cancer Sci. 2018;109:1743-1752.
12. Yang J, Li Y, Liu Q, et al. Brief introduction of medical database and data mining technology in big data era. J Evid Based Med. 2020;13(1):57-69. doi:10.1111/jebm.12373
13. Bo YC, Song C, Wang JF, Li XW. Using an autologistic regression model to identify spatial risk factors and spatial risk patterns of hand, foot and mouth disease (HFMD) in Mainland China. BMC Public Health. 2014;14:358. doi:10.1186/1471-2458-14-358
14. D’Angelo E, Prat J. Uterine sarcomas: a review. Gynecol Oncol. 2010; 116(1):131-139. doi:10.1016/j.ygyno.2009.09.023
15. Arend RC, Toboni MD, Montgomery AM, et al. Systemic treatment of metastatic/recurrent uterine Leiomyosarcoma: a changing paradigm. Oncologist. 2018;23(12):1533-1545. doi:10.1634/theoncologist.2018-0095
16. Mankin HJ, Casas-Ganem J, Kim JL, Gebhardt MC, Hromicek FJ, Zeegen EN. Leiomyosarcoma of somatic soft tissues. Clin Orthop Relat Res. 2004 Apr;421:225-231. doi:10.1097/01.blo.0000119250.08614.82
17. Coindre JM, Terrier P, Guillou L, et al. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group. Cancer. 2001;91(10):1914-1926. doi:10.1002/1097-0142(20010515)91:10<1914::AID-CNCR1214>3.0.CO;2-3
18. Keung EZ, Chiang YJ, Voss RK, et al. Defining the incidence and clinical significance of lymph node metastasis in soft tissue sarcoma. Eur J Surg Oncol. 2018;44(1):170-177. doi:10.1016/j.ejos.2017.11.014
19. Lamm W, Natter C, Schur S, et al. Distinctive outcome in patients with non-uterine and uterine leiomyosarcoma. BMC Cancer. 2014;14:981. doi:10.1186/1471-2407-14-981
20. Cahlon O, Brennan MF, Jia X, Qin LX, Singer S, Alektiar KM. A post-operative nomogram for local recurrence risk in extremity soft tissue sarcomas after limb-sparing surgery without adjuvant radiation. Ann Surg. 2012;255(2):343-347. doi:10.1097/SLA.0b013e3182367aa7
21. Kazlouskaya V, Lai YC, Khachemoune A. Leiomyosarcoma of the skin: review of the literature with an emphasis on prognosis and management. Int J Dermatol. 2020;59(2):165-172. doi:10.1111/ijd.14705
22. Trovik CS, Bauer HC, Alvegård TA, et al. Surgical margins, local recurrence and metastasis in soft tissue sarcomas: 559 surgically-treated patients from the Scandinavian Sarcoma Group Register. Eur J Cancer. 2000;36(6):710-716. doi:10.1016/s0959-8049(99)00287-7
23. Tan MC, Brennan MF, Kuk D, et al. Histology-based classification predicts pattern of recurrence and improves risk stratification in primary retroperitoneal sarcoma. Ann Surg. 2016;263(3):593-600. doi:10.1097/SLA.0000000000001149
24. Iasonos A, Keung EZ, Zivanovic O, et al. External validation of a prognostic nomogram for overall survival in women with uterine leiomyosarcoma. Cancer. 2013;119(10):1816-1822. doi:10.1002/cncr.29771
25. Mancari R, Signorelli M, Gadducci A, et al. Adjuvant chemotherapy in stage I-II uterine leiomyosarcoma: a multicentric retrospective study of 140 patients. Gynecol Oncol. 2014;133(3):531-536. doi:10.1016/j.ygyno.2014.03.001
26. Ricci S, Giuntoli RL 2nd, Eisenhauer E, et al. Does adjuvant chemotherapy improve survival for women with early-stage uterine leiomyosarcoma? Gynecol Oncol. 2013;131(3):629-633. doi:10.1016/j.ygyno.2013.08.037
27. Zhang L, Gong Z. Clinical characteristics and prognostic factors in bone metastases from lung cancer. Med Sci Monit. 2017;23:4087-4094. doi:10.12659/msm.902971

How to cite this article: Li Z, Wei J, Cao H, Song M, Zhang Y, Jin Y. Development, validation, and visualization of a web-based nomogram for predicting the incidence of leiomyosarcoma patients with distant metastasis. Cancer Reports. 2022;5(5):e1594. doi:10.1002/cnr2.1594