Development and validation of prognostic nomograms for pseudomyxoma peritonei patients after surgery

A population-based study

Peng Chen, MM\(^a\), Lan Su, MM\(^b\), Wenming Yang, MM\(^a\), Jianhao Zhang, MM\(^a\), Yong Wang, MD\(^{a,c}\), Cun Wang, MD\(^{a,c}\), Yongyang Yu, MD\(^{a,c,\ast}\), Lie Yang, MD\(^{a,c,d,\ast}\), Zongguang Zhou, MD\(^{a,c}\)

Abstract

Background: The aim of study was to develop and validate nomograms for predicting overall survival (OS) and cancer-specific survival (CSS) of patients with pseudomyxoma peritonei (PMP) and compare the predictive accuracy with the American Joint Committee on Cancer (AJCC) staging system.

Methods: Data of 4959 PMP patients who underwent surgical resection were collected between 2004 and 2015 from the Surveillance Epidemiology and End Results (SEER) database. All included patients were divided into training (n=3307) and validation (n=1652) cohorts. The Kaplan-Meier method and Cox proportional hazard model were applied. Nomograms were validated by discrimination and calibration. Finally, concordance index (C-index) was used to compare the predictive performance of nomograms with that of the AJCC staging system.

Results: According to the univariate and multivariate analyses of training sets, both nomograms for predicting OS and CSS combining age, grade, location, N stage, M stage, and chemotherapy were identified. Nomograms predicting OS also incorporated T stage and the number of lymph nodes removed (LNR). The calibration curves showed good consistency between predicted and actual observed survival. Moreover, C-index values demonstrated that the nomograms predicting both OS and CSS were superior to the AJCC staging system in both cohorts.

Conclusion: We successfully developed and validated prognostic nomograms for predicting OS and CSS in PMP patients. Two nomograms were more accurate and applicable than the AJCC staging system for predicting patient survival, which may help clinicians stratify patients into different risk groups, tailor individualized treatment, and accurately predict patient survival in PMP.

Abbreviations: AJCC = American Joint Committee on Cancer, C-index = concordance index, CRS = cytoreduction surgery, CSS = cancer specific survival, DFS = disease free survival, HIPEC = hyperthermic intraperitoneal chemotherapy, ICD-O-3 = The International Classification of Diseases for Oncology, third edition, LNR = lymph nodes removed, OS = overall survival, PMP = pseudomyxoma peritonei, RCT = Randomized Controlled Trial, SEER = Surveillance Epidemiology and End Results; TNM = Primary tumor (T), Regional lymph nodes (N) and Distant metastasis (M).

Keywords: cancer-specific survival, nomogram, overall survival, pseudomyxoma peritonei
1. Introduction

Pseudomyxoma peritonei (PMP), first proposed by James Werth in 1884, is characterized by mucinous ascites in the abdomen with mucinous implants on the peritoneal surface.\cite{1,2} The estimated incidence of PMP is approximately 1 to 4 individuals per million per year.\cite{3} Since the behavior of PMP is largely indolent and left untreated, which is associated with 10-year survival rates between 33% and 68%.\cite{4,5} Current recommended standard treatment for PMP includes complete cytoreduction surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).\cite{6} With CRS and HIPEC, researches have reported 5-year survival rates of 43% to 83%\cite{7–13} and 5-year DFS rates of 43% to 56%.\cite{11,14} The recurrence rate following CRS and HIPEC was 18.6% to 46%\cite{8,15–17}.

Although great efforts have been made previously to improve PMP prognosis, it is difficult in accurately estimating the prognosis of PMP using 1 single index because many factors may affect the prognosis of PMP, including sex, age, TNM stage, tumor differentiation, tumor location, radiotherapy, and chemotherapy. Thus, it is imperative to establish a new accurate prognostic tool, which can integrate all significant factors to accurately predict individual patient outcomes.

Nomograms have been widely accepted as easy-to-use and reliable predictive tools and are constructed in several tumors.\cite{18–20} Nomogram provide an individual estimate of patient survival by incorporating and illustrating all important prognostic factors. However, no published prognostic nomograms have been reported for PMP patients based on population-based data. Thus, this study aimed to construct a prognostic nomogram for PMP based on large-scale population data from the Surveillance, Epidemiology and End Results (SEER) program database.

2. Patients and methods

2.1. Patient selection from the SEER database

All data were collected from the SEER database, which gathers clinical information concerning cancer prevalence, incidence, management, and associated prognostic studies from 18 registries in the USA and covers nearly 28% of US population.\cite{21}

We used SEER * Stat software (Version 8.3.5) to obtain data from patients diagnosed with PMP as first primary malignancy between 2004 and 2015. The cohort for this analysis included adult patients (≥20 years) diagnosed with PMP who underwent radical surgery. The International Classification of Diseases for Oncology, third edition (ICD-O-3) was used to identify PMP cases. The following ICD-O-3 codes including PMP were used: 8480/3.

The following patients were excluded: patients aged <20 years; those diagnosed at autopsy or after death and those without radical resection surgery or surgery unknown; those with incomplete information (such as grade, race, cause of death, TNM classification, and staging information); and those who did not receive radiation therapy and survived <1 month. A total of 4959 patients with PMP who underwent surgical resection were randomly and inconsistently divided into the training (n=3307) and validation (n=1652) cohorts. Patient selection is shown in a flow diagram (Fig. 1).

2.2. Variables

For each patient, the following data were acquired: year of diagnosis, age at diagnosis, first malignancy primary indicator, sex, race, differentiation, primary tumor location, AJCC Stage Group (7th edition), AJCC T stage, N stage, and M stage (7th edition), primary surgery, the number of lymph nodes removed (LNR), chemotherapy and radiotherapy information, survival information, and cause of death. Patient age was divided into 3 groups, using the X-tile program to get the best cut-off points (Fig. 2). Then age at diagnosis was classified into 3 categories: “20–64 years,” “65–74 years,” and “≥75 years.” Patients in the SEER database who were classified as American Indians, Alaska Aboriginal, Asians, or Pacific Islanders were defined as “Others” race category while performing the analysis. Our primary endpoint was overall survival (OS) and cancer-specific survival (CSS). We defined OS as the time interval from PMP diagnosis to
death from any cause and CSS as the period from PMP diagnosis to death from PMP (CSS).

### 2.3. Development of nomograms

All categorical variables are expressed as frequencies and proportions. The Kaplan–Meier and Cox proportional hazards regression models were adopted to identify significant prognostic factors. Only factors that were significantly associated with survival in the univariate analysis were included in the multivariate analysis (significance with 2-sided \( P < .05 \)). The results in the multivariate analyses were applied to construct nomograms for predicting the 1-, 3-, and 5-year OS and CSS.

### 2.4. Validation of nomograms

The predictive performance of nomograms was validated both internally (training cohort) and externally (validation cohort) by discrimination and calibration.\(^{[22]}\) Discrimination was evaluated by Harrell concordance index (C-index). C-index was used to evaluate the predictive performance. The C-index is used to evaluate the predictive performance and is similar to AUC calculation, but seems to be more suitable for censored data.\(^{[24]}\) The C-index value varied between 0.5 (random chance) and 1.0 (totally corrected discrimination).\(^{[20]}\) A calibration plot was used to determine whether the predicted survival was in concordance with actual survival.

### 2.5. Statistical analysis

All the statistical analyses were conducted using R software version 3.5.1 (http://www.r-project.org). The Kaplan–Meier method and Cox proportional hazard model were used to identify significant prognostic factors. The “rms” package of R software was adopted to develop and validate the nomogram.\(^{[21]}\) The bilateral \( P \) values \(< .05 \) were considered statistically significant.

## 3. Results

### 3.1. Patient characteristics

Between 2004 and 2015, 4959 patients who underwent surgical resection were enrolled in the present study. Patients were randomly and inconsistently categorized into training (\( n = 3307 \)) and validation (\( n = 1652 \)) cohorts. Figure 1 lists the data selection process. Demographic and clinicopathological characteristics between the 2 groups are listed in Table 1.

### 3.2. Development of nomograms

Univariate and multivariate Cox proportional hazard model analyses were conducted to identify independent survival-related factors of OS and CSS in the training cohort. In univariate analysis, age, sex, grade, location, stage, T stage, N stage, M stage, LNR, chemotherapy, and radiotherapy were significantly associated with OS in the training cohort (\( P < .05 \)). To control potential confounding factors, multivariate analysis identified age, grade, location, T stage, N stage, M stage, LNR, and chemotherapy as independent prognostic factors (Table 2). These factors were then incorporated to create a prognostic nomogram for estimating the 1-, 3-, and 5-year OS and CSS (Fig. 3).

### 3.3. Validation of nomograms

The predictive performance of nomograms was evaluated by C-index via internal and external validation. The analysis of the internal validation cohort demonstrated that the C-index of nomograms was 0.757 (95% CI, 0.745–0.769) for OS and 0.645 (95% CI, 0.627–0.663) for CSS (Table 4). The external validation analysis conducted via the validation cohort demonstrated the C-index of nomograms as 0.746 (95% CI, 0.728–0.764) for OS and 0.638 (95% CI, 0.614–0.662) for CSS. Calibration curves showed good concordance between predicted and actual observed 1-, 3-, and 5-year OS and CSS in both training and validation cohorts (Figs. 5 and 6).

Furthermore, C-index was used to compare the predictive performance between nomograms and AJCC staging system and prediction of both OS and CSS with nomograms was superior to that with the AJCC staging system in both cohorts (Table 4).
4. Discussion

To date, there is no comprehensive nomogram for PMP. In this study, we developed prognostic nomograms to predict the 1-, 3-, and 5-year OS and CSS of PMP patients based on a large-scale, multicentre dataset from the SEER database. Our nomograms displayed favorable discrimination and calibration. Furthermore, the nomogram showed better prediction accuracy than the traditional TNM staging system. For example, two stage III PMP patients: the first patient who is 75 years old with a grade IV tumor located at ovary and the other patient who is a 65 years old with a grade I tumor located at appendix. According to TNM staging, both 2 patients had a same prognosis. However, using the nomograms, the 2 patients have 5-year OS probabilities of near 35% and above 90%, respectively (Fig. 3).

Table 1

| Characteristic                  | Training cohort (n=3307) | Validation cohort (n=1652) | All patients (n=4959) |
|--------------------------------|-------------------------|---------------------------|----------------------|
|                                | No.        | %   | No.       | %   | No.       | %   |
| Age at diagnosis, y            |            |     |            |     |            |     |
| 20–64                          | 1672       | 50.6| 815       | 49.3| 2487      | 50.2|
| 65–74                          | 791        | 23.9| 430       | 26.0| 1221      | 24.6|
| ≥75                            | 844        | 25.5| 407       | 24.6| 1251      | 25.2|
| Gender                         |            |     |            |     |            |     |
| Male                           | 1547       | 46.8| 1121      | 54.3| 2302      | 46.4|
| Female                         | 1760       | 53.2| 943       | 45.7| 2657      | 53.6|
| Race                           |            |     |            |     |            |     |
| White                          | 2573       | 77.8| 1322      | 80.0| 3895      | 78.5|
| Black                          | 453        | 13.1| 181       | 11.0| 614       | 12.4|
| Others                         | 301        | 9.1 | 149       | 9.0 | 450       | 9.1 |
| Grade                          |            |     |            |     |            |     |
| I                              | 376        | 11.4| 186       | 11.3| 562       | 11.3|
| II                             | 1928       | 58.3| 986       | 58.0| 2886      | 58.2|
| III                            | 814        | 24.6| 420       | 25.4| 1234      | 24.9|
| IV                             | 189        | 5.7 | 88        | 5.3 | 277       | 5.6 |
| Chemotherapy                   |            |     |            |     |            |     |
| No                             | 1020       | 31.1| 502       | 30.4| 1531      | 30.9|
| Yes                            | 2278       | 68.9| 1150      | 69.6| 3428      | 69.1|
| Radiotherapy                   |            |     |            |     |            |     |
| No                             | 2663       | 80.5| 1322      | 80.0| 3985      | 80.4|
| Yes                            | 644        | 19.5| 330       | 20.0| 974       | 19.6|
| Primary tumor location         |            |     |            |     |            |     |
| Others                        | 457        | 13.8| 224       | 13.6| 681       | 13.7|
| Ovary                         | 22         | 0.7 | 5         | 0.3 | 27        | 0.5 |
| Appendix                       | 94         | 2.8 | 41        | 2.5 | 135       | 2.7 |
| Pancreas and gallbladder       | 70         | 2.1 | 52        | 3.1 | 122       | 2.5 |
| Intestine tract                | 2664       | 80.6| 1330      | 80.5| 3994      | 80.5|
| AJCC TNM stage                 |            |     |            |     |            |     |
| Stage I                        | 32         | 1.0 | 14        | 0.8 | 46        | 0.9 |
| Stage II                       | 247        | 7.5 | 130       | 7.9 | 377       | 7.6 |
| Stage III                      | 2254       | 68.2| 1086      | 65.7| 3340      | 67.4|
| Stage IV                       | 774        | 23.4| 422       | 25.5| 1196      | 24.1|
| T stage                        |            |     |            |     |            |     |
| T1                             | 162        | 4.9 | 71        | 4.3 | 233       | 4.7 |
| T2                             | 311        | 9.4 | 176       | 10.7| 487       | 9.8 |
| T3                             | 1741       | 52.6| 872       | 52.8| 2613      | 52.7|
| T4                             | 1093       | 33.1| 533       | 32.3| 1626      | 32.8|
| N stage                        |            |     |            |     |            |     |
| N1                             | 1923       | 58.1| 985       | 59.6| 2908      | 58.6|
| N2                             | 1328       | 40.2| 638       | 38.6| 1966      | 39.6|
| N3                             | 56         | 1.7 | 29        | 1.8 | 85        | 1.7 |
| M stage                        |            |     |            |     |            |     |
| M0                             | 2549       | 77.1| 1241      | 75.1| 3790      | 76.4|
| M1                             | 758        | 22.9| 411       | 24.9| 1169      | 23.6|
| LNR (Lymph node removed)       |            |     |            |     |            |     |
| None                           | 352        | 10.6| 166       | 10.0| 518       | 10.4|
| 1–3 removed                    | 78         | 2.4 | 53        | 3.2 | 131       | 2.6 |
| ≥4 removed                     | 2877       | 87.0| 1433      | 86.7| 4310      | 86.9|

AJCC = American Joint Committee on Cancer.
* Others includes American Indian/Alaskan Native and Asian/Pacific Islander.
† Others includes esophagus, appendix, and peritoneum.
The nomograms highlighted the clinical predictive value of age, grade, location, N stage, M stage, and chemotherapy in PMP patients. Several studies have reported older age as an independent risk factor, revealing that elderly patients have lower survival rates.\(^{[25–27]}\) Our results also recognized advanced age as an independent risk factor while predicting OS and CSS of PMP patients. In accordance with our findings, previous studies have demonstrated that the average age when PMP occurs is 53 years.\(^{[28,29]}\) Furthermore, age is a crucial survival-related factor in patients with PMP.\(^{[30]}\) In addition, tumor differentiation degree is an important prognostic factor in cancer patients.\(^{[9,16,31,32]}\) Our result also indicated that poor differentiation has a poor prognosis.

As for the location of origin of PMP, 1 study reported that the predominant primary site is mucinous appendiceal adenocarcinoma and that PMP prognosis also varies with the site of origin. The table below summarizes the univariate and multivariate analyses of overall survival in the training cohort.

| Prognostic factor                           | Univariable analysis | Multivariable analysis |
|--------------------------------------------|----------------------|------------------------|
|                                            | HR (95% CI)         | P         | HR (95% CI)         | P         |
| Age at diagnosis, y                        |                      |           |                      |           |
| 20–64 Reference                             |                      |           |                      |           |
| 65–74                                      | 1.234 (1.080–1.409) | .002      | 1.291 (1.128–1.478) | <.001     |
| ≥75                                        | 2.041 (1.812–2.298) | <.001     | 2.138 (1.874–2.439) | <.001     |
| Gender                                     |                      |           |                      |           |
| Female Reference                           |                      |           |                      |           |
| Male                                       | 1.142 (1.03–1.266)  | .012      | 1.09 (0.979–1.214)  | .118      |
| Race                                       |                      |           |                      |           |
| White Reference                            |                      |           |                      |           |
| Black                                      | 0.927 (0.792–0.699) | .347      | 0.846 (0.699–1.024) | .087      |
| Others*                                    |                      |           |                      |           |
| Grade                                      |                      |           |                      |           |
| Grade I Reference                          |                      |           |                      |           |
| Grade II                                   | 1.254 (1.039–1.515) | .018      | 1.072 (0.882–1.303) | .487      |
| Grade III                                  | 2.032 (1.667–2.476) | <.001     | 1.391 (1.132–1.710) | .002      |
| Grade IV                                   | 1.974 (1.520–2.503) | <.001     | 1.181 (0.900–1.549) | .229      |
| Primary tumor location                     |                      |           |                      |           |
| Others*                                    |                      |           |                      |           |
| Ovary                                      | 4.775 (2.871–7.941) | <.001     | 4.078 (2.336–7.117) | <.001     |
| Appendix                                   | 2.292 (1.616–3.251) | <.001     | 0.580 (0.385–0.878) | .009      |
| Pancreas and Gallbladder                   | 3.885 (2.803–5.386) | <.001     | 3.160 (2.128–4.690) | <.001     |
| Intestine tract                            | 2.021 (1.672–2.441) | <.001     | 0.714 (0.547–0.958) | .024      |
| AJCC TNM stage stage                       |                      |           |                      |           |
| Stage I                                    | 2.823 (1.884–9.015) | .07976    | 1.613 (0.478–5.440) | .441      |
| Stage II                                   | 4.574 (1.472–14.215)| .009      | 2.079 (0.622–6.954) | .235      |
| Stage IV                                   | 15.577 (5.008–48.451)| <.001     | 1.710 (0.424–6.888) | .451      |
| T stage                                   |                      |           |                      |           |
| T1                                         | 1.125 (0.753–1.682) | .565      | 0.917 (0.601–1.399) | .688      |
| T2                                         | 2.054 (1.469–2.872) | <.001     | 1.275 (0.875–1.859) | .206      |
| T3                                         | 4.076 (2.913–5.703) | <.001     | 1.959 (1.337–2.869) | <.001     |
| N stage                                   |                      |           |                      |           |
| N1                                         | 1.926 (1.735–2.138) | <.001     | 1.677 (1.498–1.877) | <.001     |
| N2                                         | 1.598 (1.080–2.364) | .019      | 2.025 (1.346–3.047) | <.001     |
| M stage                                   |                      |           |                      |           |
| M0                                         | 3.642 (2.373–4.051) | <.001     | 4.25 (2.104–8.586)  | <.001     |
| LNR (lymph node removed)                  |                      |           |                      |           |
| None                                       | 3.774 (2.613–5.451) | <.001     | 2.622 (1.714–4.009) | <.001     |
| ≥4 removed                                 | 2.672 (2.108–3.388) | <.001     | 1.763 (1.274–2.440) | <.001     |
| Chemotherapy                               |                      |           |                      |           |
| No                                         | 0.547 (0.492–0.608) | <.001     | 0.478 (0.425–0.537) | <.001     |
| Yes                                        | 0.583 (0.504–0.675) | <.001     | 0.947 (0.807–1.111) | .500      |

AJCC = American Joint Committee on Cancer.

*Others includes American Indian/Alaskan Native and Asian/Pacific Islander.

b Others includes esophagus, appendix, and peritoneum.
Previous studies have reported that PMP is commonly found in mucinous tumors of the ovary and appendix, but rarely in mucinous tumors of several other organs, including the gallbladder and bile ducts, pancreas, stomach, colon, fallopian tubes, uterus, urachus, urinary bladder, breasts, and lungs.\(^{13,14,35–38}\) Our result indicated that cases of PMP originating from the ovary, pancreas, gallbladder, and other location are associated with a decreased overall survival rate compared with those originating from the appendix and intestinal tract. The correlation between tumor origin and patient prognosis in PMP was uncertain before and our results have provided some evidence on this topic.

The AJCC staging system is the most widely used system for predicting outcome of patients with cancer. Similarly, our

### Table 3
Univariate and multivariate analyses of cancer-specific survival in the training cohort.

| Prognostic factor | Univariable analysis | Multivariable analysis |
|-------------------|----------------------|------------------------|
|                   | HR (95% CI)          | P          | HR (95% CI) | P          |
| **Age at diagnosis, y** |                     |             |             |             |
| 20–64             | Reference            | Reference   |
| 65–74             | 1.237 (1.076–1.423)  | .003       | 1.213 (1.052–1.398) | .008      |
| ≥75               | 1.593 (1.398–1.817)  | <.001      | 1.483 (1.283–1.713) | <.001      |
| **Gender** |                     |             |             |             |
| Female            | Reference            | Reference   |
| Male              | 0.930 (0.832–1.04)   | .202       |             |             |
| **Race** |                     |             |             |             |
| White             | Reference            | Reference   |
| Black             | 1.033 (0.872–1.225)  | .705       |             |             |
| Others*           | 0.969 (0.789–1.191)  | .765       |             |             |
| **Grade** |                     |             |             |             |
| I                 | Reference            | Reference   |
| II                | 1.130 (0.913–1.390)  | .262       | 1.318 (1.056–1.645) | .014      |
| III               | 1.321 (1.058–1.650)  | .014       | 1.517 (1.225–1.938) | <.001      |
| IV                | 1.190 (0.895–1.582)  | .231       | 1.406 (1.048–1.887) | .023       |
| **Primary tumor location** |                 |             |             |             |
| Othersb           | Reference            | Reference   |
| Ovary             | 1.827 (1.090–3.061)  | .022       | 2.939 (1.727–5.003) | <.001      |
| Appendix          | 1.181 (0.819–1.704)  | .373       | 1.032 (0.707–1.507) | .871       |
| Pancreas and gallbladder | 1.236 (0.872–1.753) | .234     | 1.774 (1.239–2.540) | .002       |
| Intestine tract   | 1.126 (0.914–1.388)  | .266       | 0.966 (0.771–1.211) | .765       |
| **AJCC TNM stage** |                     |             |             |             |
| Stage I           | Reference            | Reference   |
| Stage II          | 0.928 (0.687–1.252)  | .623       |             |             |
| Stage III         | 1.221 (0.904–1.640)  | .193       |             |             |
| Stage IV          | –                    | –           |             |             |
| **T stage** |                     |             |             |             |
| T1                | Reference            | Reference   |
| T2                | 1.226 (0.762–1.973)  | .402       |             |             |
| T3                | 1.265 (0.847–1.888)  | .251       |             |             |
| T4                | 1.470 (0.985–2.194)  | .060       |             |             |
| **N stage** |                     |             |             |             |
| N1                | Reference            | Reference   |
| N2                | 1.220 (1.090–1.366)  | <.001      | 1.338 (1.186–1.508) | <.001      |
| N3                | 1.311 (0.878–1.958)  | .185       | 1.546 (1.023–2.337) | .039       |
| **M stage** |                     |             |             |             |
| M0                | Reference            | Reference   |
| M1                | 1.328 (1.186–1.486)  | <.001      | 1.578 (1.397–1.783) | <.001      |
| **LNR (lymph node removed)** |                |             |             |             |
| None              | Reference            | Reference   |
| 1–3 removed       | 1.019 (0.682–1.524)  | .925       |             |             |
| ≥4 removed        | 1.028 (0.784–1.348)  | .840       |             |             |
| **Chemotherapy** |                     |             |             |             |
| No                | Reference            | Reference   |
| Yes               | 0.571 (0.509–0.642)  | <.001      | 0.563 (0.494–0.642) | <.001      |
| **Radiotherapy** |                     |             |             |             |
| No                | Reference            | Reference   |
| Yes               | 0.689 (0.59–0.803)   | <.001      | 0.852 (0.719–1.010) | .065       |

AJCC = American Joint Committee on Cancer.

* Others includes American Indian/Alaskan Native and Asian/Pacific Islander.

b Others includes esophagus, appendix, and peritoneum.
nomogram also showed that the T/N/M categories were good independent prognostic indicators. Besides, several studies have confirmed and recommended that radical surgery or CRS with HIPEC are optimal treatments for PMP patients,[39–41] and this was consistent with our findings. It suggests that radical surgery or CRS and chemotherapy (HIPEC) are the best treatment options for PMP patients. Additionally, because a vast majority of patients in the SEER database underwent radical surgery, this study failed to explore the relationship between surgery or no surgery or the degree of surgical resection and patient prognosis.

In addition, the nomogram for predicting 1-, 3-, and 5-year OS also incorporated LNR as a prognosis factor. We found that PMP patients with LNR=0 had better prognosis of OS than patients with LNR≠0, which was statistically significant difference; the reason may be that the lymph node had no tumor metastasis. Moreover, PMP patients with an LNR number of 1 to 3 had worse prognosis than those with LNR number ≥4 in our study.

Figure 3. A nomogram to predict 1-, 3-, and 5-year overall survival (OS) of patients with pseudomyxoma peritonei.

Figure 4. A nomogram to predict 1-, 3-, and 5-year cancer-specific survival (CSS) of patients with pseudomyxoma peritonei.
This may be because for PMP patients with an LNR number of 1 to 3, lymph nodes may have been incompletely removed, resulting in residual lymph nodes with tumor metastasis. However, sex, race, AJCC stage, and radiotherapy were not found to be prognostic factors.

In general, our study has several merits. First, to the best of our knowledge, this study pioneers the use of nomograms for predicting OS and CSS of PMP patients based on a large population-based cohort. Second, using C-index, we found that the established nomograms are more accurate and applicable than the AJCC TNM staging system (7th edition) in PMP patients. Nevertheless, our study has several limitations. First, considering that this is a retrospective study, this study may lead to the risk of potential patient selection bias. Therefore, large-scale, randomized, and controlled studies are warranted. Second, information on the mutation of the K-Ras gene or P53 gene, as well as some positive clinicopathological characteristics associated with prognosis such as data concerning recurrence and detailed data on the specific cause of death of PMP patients, was not available in the SEER database and thus could not be integrated in our analysis.

5. Conclusion
We successfully developed and validated prognostic nomograms to predict the survival of PMP patients based on a large population-based cohort. The 2 nomograms established in this study were more accurate and applicable than the AJCC staging system for predicting survival. Accordingly, these could help clinicians stratify patients with different risks, tailor individualized treatment and follow-up plans, and accurately predict patient survival in PMP.

### Table 4
Comparison of C-indexes between the nomogram and TNM stages in patients with PMP.

| Survival | Training cohort | Validation cohort |
|----------|-----------------|-------------------|
|          | HR  | 95% CI | HR  | 95% CI |
| OS       |     |        |     |        |
| Nomogram | 0.757 | 0.745–0.769 | 0.746 | 0.728–0.764 |
| AJCC TNM seventh stage | 0.639 | 0.625–0.653 | 0.635 | 0.617–0.653 |
| CSS      |     |        |     |        |
| Nomogram | 0.645 | 0.627–0.663 | 0.638 | 0.614–0.662 |
| AJCC TNM seventh stage | 0.537 | 0.521–0.553 | 0.556 | 0.534–0.578 |

AJCC=American Joint Committee on Cancer; CSS=overall specific survival; OS=overall survival; PMP=pseudomyxoma peritonei.

Figure 5. Calibration plots of the nomogram for 1-, 3-, and 5-year overall survival (OS) prediction of the training cohort (A–C) and validation cohort (D–F).
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Author contributions
Conceptualization: Lie Yang, Yongyang Yu.
Data curation: Peng Chen, Wenming Yang, Lan Su.
Formal analysis: Lie Yang, Yongyang Yu.
Funding acquisition: Lie Yang.
Methodology: Peng Chen, Wenming Yang, Lie Yang, Yongyang Yu.
Project administration: Lie Yang.
Software: Peng Chen, Wenming Yang, Lan Su.
Supervision: Lie Yang, Yongyang Yu.
Writing – original draft: Peng Chen.
Writing – review & editing: Lie Yang, Yongyang Yu, Yong Wang, Cun Wang, Zongguang Zhou.

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