Nomogram to predict overall survival of patients with pseudomyxoma peritonei of appendiceal origin: A retrospective cohort study

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Abstract

Background: Pseudomyxoma peritonei (PMP) is a rare disease, with the rate of overall survival (OS) influenced by many factors. The present study aimed to define independent predictors and establish a nomogram for individual risk prediction in PMP patients.

Methods: One hundred forty-seven PMP patients were consecutively included between June 1, 2013, and November 22, 2019. The log-rank test was used to compare the OS rate between groups; subsequently, variables with \( p < .10 \) were subjected to multivariate Cox modeling for defining independent prediction indicators. Finally, a nomogram was established based on independent prognosticators and assessed for internal validation.

Results: Multivariate Cox analysis showed that D-dimer level, carbohydrate antigen (CA) 125 level, CA 19-9 level, degree of radical surgery, and histological grade were all independently associated with OS in PMP patients. A nomogram was plotted and underwent internal validation. The discrimination ability of the nomogram revealed a good predictive ability as indicated by the C-index value (0.825), and calibration plots confirmed good consistency between the predicted and observed survival probabilities.

Conclusions: Five independent prognostic factors for predicting the survival of PMP patients were identified, and the nomogram based on these independent indicators showed a reasonable discrimination ability for individual risk prediction.

KEYWORDS
nomogram, overall survival, pseudomyxoma peritonei

1 | INTRODUCTION

Pseudomyxoma peritonei (PMP) is a rare disease characterized by disseminated mucinous ascites within the peritoneal cavity, which most often originates from a perforated appendiceal epithelial neoplasm.1 Smeenk et al.2 estimated the incidence of PMP to be about two cases per one million people annually in the Netherlands, while other major research centers have suggested that the actual incidence may be higher at 3-4 operable cases per one million people per year.3 More recently, cytoreductive surgery (CRS) in combination
with hyperthermic intraperitoneal chemotherapy (HIPEC) has been recommended as the optimal treatment for PMP; as a result, the recurrence rate has decreased and the overall survival (OS) has improved greatly.

Although the long-term outcomes after treatment are impressive in patients with PMP, there is still a significant rate of recurrence of the disease. It has been confirmed that many factors—for instance, male sex, high tumor marker levels, high-grade mucinous carcinoma peritonei (especially with signet ring cells), debulking surgery, and even KRAS mutation—were all independently associated with poor prognosis in PMP. A recent study constructed a nomogram to predict the OS for PMP patients based on large-scale population data from the Surveillance, Epidemiology and End Results (SEER) program database, where the C-index was 0.757 in the training cohort and 0.746 in the validation cohort. To our knowledge, this is the first established prognostic nomogram for PMP; however, because this nomogram was constructed using a population-based cancer database, the availability of predictive factors is limited and some bioinformatics factors, such as tumor markers, that have been proven to be predictive for PMP patients were not included in the study.

In the present study, we intended to evaluate more comprehensive candidate prognostic factors to predict the OS for PMP patients, which were selected a priori based on either prior research (e.g., sex, carcinoembryonic antigen [CEA], carbohydrate antigen [CA] 125, CA 19-9, degree of radical surgery, and histological grade) or sound clinical reasoning [e.g., age, Barthel Index Score, hemoglobin, albumin, d-dimer, CA 724, CA 242, and peritoneal cancer index (PCI)]. Using this foundation, we sought to create and internally validate a nomogram to predict the individual risk of OS for PMP patients, which may be helpful for physicians involved in the prognosis judgment and treatment of PMP patients.

### MATERIALS AND METHODS

#### 2.1 Patients

The institutional review board (IRB) of Aerospace Central Hospital approved the present study (ethics no. 20200113‐LCYJ‐01), and all of the patients signed informed consent before CRS and consented to be followed up with after surgery.

This was a retrospective study. We retrieved cases with a diagnosis of PMP in the special follow‐up database from Aerospace Central Hospital between June 1, 2013, and November 22, 2019. The PMP diagnosis was finally confirmed based on histological results of resected specimens, which were interpreted by two experienced pathologists according to the Peritoneal Surface Oncology Group International (PSOGI) criteria. The study inclusion criteria were patients who received CRS and HIPEC treatment at our center for the first time (n = 160). The exclusion criteria were as follows: (1) patients with incomplete medical records (n = 1); (2) PMP of nonappendiceal origin [i.e., colorectal (n = 5), urachal (n = 1), biliary pancreatic (n = 1), or ovary (n = 1)]; (3) combined with other malignant tumors (n = 1 subject with breast and thyroid cancer); or (4) lost to follow‐up by November 8, 2020 (n = 3). Ultimately, 147 PMP patients were included in the present study; the study schematic is shown in Figure 1.

#### 2.2 Follow‐up protocol

All patients were routinely followed up with every 3–6 months after having undergone CRS and HIPEC for the first time, and tumor markers and computed tomography (CT) imaging of the abdominopelvic region were routinely examined. Most patients routinely came to our center for follow‐up; however, if the patient did not visit our center for follow‐up, we assessed them by telephone to determine the patient’s survival status.

![FIGURE 1 Study schematic. A total of 160 patients with PMP who underwent CRS and HIPEC at our center for the first time were included. Among the 160 identified cases, one with incomplete medical records, eight with disease of non-appendiceal origin [colorectal (n = 5), urachal (n = 1), biliary pancreatic (n = 1), and ovary (n = 1)], one combined with breast and thyroid cancer, and three lost to follow-up were all excluded. Ultimately, 147 subjects with PMP were included in the present study. CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy; PMP, pseudomyxoma peritonei.](image-url)
2.3 | Endpoint event determination

The time of CRS was taken as the starting time for follow-up. All-cause mortality served as an endpoint event in the present study. The final date of follow-up was November 8, 2020.

2.4 | Tumor markers determination

All tumor markers were determined within seven days before CRS. All measurements were performed according to manufacturer's instructions. CEA (ng/ml), CA 125 (U/ml), and CA 19-9 (U/ml) were measured by chemiluminescence immunoassay (CMIA) (Abbott), the detection method of CA 724 (U/ml) was same as the former three tumor markers (Autobio, Zhengzhou, China), while CA 242 (kU/L) was measured by flow fluorescent technology (Luminex). Internal quality control (IQC) and external quality assessment (EQC) were all performed for all five tumor markers.

2.4.1 | Peritoneal cancer index

The PCI scoring system divides the abdomen into nine anatomical areas, with four further subareas of the small bowel delineated. Tumors were assessed in each area, and a score of 0–3 points was awarded for each of the 13 areas (i.e., 0 points for no tumor, 1 point for nodules <0.5 cm, 2 points for nodules between 0.5 and 5 cm, and 3 points for nodules >5 cm). The total score was then calculated by adding all the scores and ranges from zero to 39 points.15

2.5 | CRS and HIPEC

The CRS of PMP was performed consistent with standard operation method. Complete removal of all visible disease was scored as CC 0 cytoreduction, while residual disease less than 0.25 cm was scored as CC 1; both CC 0 and CC 1 are considered as having undergone complete CRS (CCRS). If the patient could not achieve complete cytoreduction, debulking treatment was performed, and any residual tumor deposit between 0.25 and 2.5 cm was scored as a CC 2 cytoreduction, while a residual tumor deposit greater than 2.5 cm was scored as CC 3 cytoreduction, and CC 2 and CC 3 were considered as having undergone maximum tumor debulking (MTD).16 Once cytoreduction was complete, intraoperative hyperthermic chemotherapy was delivered, wherein 5-fluorouracil (1000 mg) together with cisplatin (80 mg) was heated to 43°C and continuously infused using a HIPEC machine for 1 h.

2.6 | Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (version 16.0: IBM Corporation), MedCalc (version 15.2.2; MedCalc Software), X-Tile (version 3.6.1; Yale University), and R (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria). All continuous data between groups were compared using the t test or Mann–Whitney U test, as appropriate. Pearson's chi-squared test or Fisher's exact test, where appropriate, was used for the comparison of categorical data between groups.

OS was estimated from the initial date of CRS and HIPEC to death or censored at the last follow-up.17 The Kaplan–Meier method was used to describe the survival data and plot survival curves. All candidate continuous variables were processed by using the X-tile program to obtain the best cut-off points because it is easier to explain the results in clinical practice when continuous variables have been transformed into categorical variables. OS rate differences between groups were compared using the univariate log-rank test. In the present study, we performed the purposeful selection of variables to establish our prediction model for PMP patients. First, we used univariate Cox regression to screen the candidate influencing factors, and only variables with p values less than .10 were then included in multivariate Cox proportional hazard models. We defined confounding as a change in any remaining parameter estimate of more than 20% relative to the full model. A change in a parameter estimate above the specified level indicates that the excluded variable was important in the sense of providing a needed adjustment for one or more of the variables remaining in the model.15 After the independent predictors were established, the interactions between the variables were assessed in the model.

After multivariate analyses, a nomogram was constructed using the RMS package in R to visually predict the one-, two-, and 3-year OS rates for PMP. The maximum score of each variable was set as 100 points. The performance of the established nomogram was measured using the Harrel concordance index (C-index) and calibration plotting. The C-index was used to assess the discrimination ability of the predicting model, and calibration plotting was used to determine whether the predicted survival was in concordance with the actual survival. The nomogram was subjected to 1000 bootstrap resamples for internal validation by discrimination and calibration. Two-sided p values less than .05 indicated a statistically significant difference.

3 | RESULTS

3.1 | Patient characteristics

Among the 160 patients who underwent CRS and HIPEC at our center for the first time, 147 subjects were finally included for survival analysis, while the remaining 13 subjects were excluded. The statistical results indicated that there was no significant difference in several key clinicopathological characteristics of the 147 subjects in comparison with the total 160 subjects (eTable in the Supplement).

The clinicopathological features of the included patients with PMP are presented in Table 1. The majority of the patients were male (66.67%), the mean age was 59 ± 10 years, and the median (interquartile range [IQR]) PCI value was 28 (21, 34). There were 12 (8.16%) patients who underwent systemic chemotherapy before
TABLE 1  Clinicopathological features of the 147 study participants with PMP

| Characteristics                  | No./level | Percent (%) |
|----------------------------------|-----------|-------------|
| Sex (men/women)                  | 98/49     | 66.67/33.33 |
| Age (years)                      | 59 ± 10   | —           |
| Disease duration (months)        | 4 (2–12)  | —           |
| Hospital stay (days)             | 25 (22–28)| —           |
| Barthel index score (points)     | 100 (95–100)| —         |
| Albumin (g/L)                    | 35.83 ± 4.87| —         |
| Hemoglobin (g/L)                 | 120 ± 18  | —           |
| d-dimer (ng/ml)                  | 562 (297–985)| —         |
| Preoperative CEA level (ng/ml)   | 23.46 (8.43–86.42)| —         |
| Preoperative CA 125 level (U/ml) | 75.30 (41.10–154.20)| —         |
| Preoperative CA 19-9 level (U/ml)| 31.31 (8.99–138.22)| —         |
| Preoperative CA 724 level (U/ml) | 75.84 (21.51–213.40)| —         |
| Preoperative CA 242 level (kU/L) | 150.00 (32.45–275.26)| —         |
| PCI                               | 28 (21–34)| —           |
| Chemotherapy before CRS          |           |             |
| No (n)                           | 135       | 91.84       |
| Yes (n)                          | 12        | 8.16        |
| Degree of radical operation      |           |             |
| CCRS (n)                         | 41        | 27.89       |
| MTD (n)                          | 106       | 72.11       |
| Pathology                        |           |             |
| Acellular mucin (n)              | 1         | 0.68        |
| DPAM (n)                         | 114       | 77.55       |
| PMCA (n)                         | 17        | 11.57       |
| PMCA-S (n)                       | 15        | 10.20       |

Abbreviations: CCRS, complete cytoreduction surgery; DPAM, disseminated peritoneal adenomucinosis; MTD, maximal tumor debulking; PMP, pseudomyxoma peritonei; PCI, peritoneal carcinomatosis index; PMCA, peritoneal mucinous carcinomatosis; PMCA-S, peritoneal mucinous carcinomatosis with signet ring cells.

A total of 61 (41.50%) deaths occurred during the follow-up period among the 147 included patients. The median survival time was 50 (95% confidence interval [CI]: 39–60) months, and the 1-, 2-, and 3-year survival rates were 85.6%, 67.4%, and 60.8%, respectively (Figure 2).

3.2 | Influence of independent prognostic variables on survival

The best cut-off points of continuous variables were calculated using the X-Tile software, and details are listed in Table 2. In univariate analysis, sex, Barthel index score, albumin, d-dimer, hemoglobin, CEA, CA 125, CA 19-9, CA 724, CA 242, PCI value, degree of radical surgery, and histological grade were all significantly associated with survival among PMP patients, while age, with a p value greater than 0.10, was not included in the multivariate analysis. After the Cox proportional hazards regression analysis, a d-dimer level greater than 449 ng/ml (hazard ratio [HR]: 2.67 [95% CI: 1.37–5.19]; p = .004), CA 125 concentration greater than 118.90 U/ml (HR: 3.52 [95% CI: 1.87–6.62]; p = .001), CA 19-9 level more than 511.23 U/ml (HR: 3.13 [95% CI: 1.52–6.45]; p = .002), MTD surgery (HR: 3.80 [95% CI: 1.76–8.22]; p = .001), and histological grade (HR: 2.04 [95% CI: 1.04–3.99]; p = .037 for PMCA or HR: 3.57 [95% CI: 1.70–7.48]; p = .001 for PMCA-S) were independently associated with poor OS in PMP patients (Table 2).

3.3 | Prognostic nomogram for OS

A nomogram that incorporated the abovementioned five significant prognostic factors was established (Figure 3), and the C-index was 0.825 (95% CI: 0.774–0.876). Furthermore, we developed a dynamic nomogram (http://127.0.0.1:7605), which demonstrated better operability to visualize statistical results than the common nomogram (Figure S1). Calibration curves (1000 bootstrap resamples) showed the existence of a good match between the actual and predicted survival probabilities (Figure 4).

4 | DISCUSSION

Reliable prognostication in any cancer after surgical resection is critical to patients and treating physicians alike for the purpose of making good decisions. The present study identified five independent prognostic factors of PMP patients and further built a nomogram to predict the OS effectively and visually. After been underwent bootstrap internal validation, the nomogram exhibited a reasonable level of predictive performance.

The particular strength of the present study is that the missing follow-up rate was very low, with only three patients lost to follow-up because, at the beginning of the establishment of our follow-up database, we had arranged for a physician to be responsible for follow-up; as such,
the low level of missed follow-up visits ensured the reliability of the research conclusion. However, the tumor load of patients was relatively high in the present research, and most patients could not obtain timely treatment; therefore, the conclusion of this study is more suitable for patients with a heavy tumor load.

A former study developed a favorable nomogram for predicting survival in PMP patients, with a C-index of 0.757 in the training cohort; meanwhile, the present research established a nomogram with a C-index of 0.825, which seems to offer a better predictive ability than that of the former study. The main reason for this difference may be that the variables included in the prediction model were different between these two studies. The former investigation was based on data from the SEER database, and some positive clinicopathological characteristics associated with prognosis were not available in the SEER database and thus could not be incorporated into the study analysis. However, our nomogram was developed based on our single-center follow-up database; so, the candidate predictors were relatively more comprehensive. In addition, the TNM staging system is not commonly used in PMP patients at our center, while PCI is commonly used for reflecting the tumor burden instead of TNM staging system.

An elevated pretreatment D-dimer level has been confirmed to be markedly associated with poor OS in patients with solid tumors, such as those with colorectal cancer, pancreatic carcinoma, and lung cancer. Interestingly, we also discovered that a high D-dimer level was associated with a poor survival prognosis in PMP patients. To our knowledge, this is the first study to evaluate the prediction value of D-dimer in PMP. In future clinical practice, clinicians should pay more attention to the D-dimer level of PMP patients.

Among the five tumor markers evaluated in the present study, CA 19-9 and CA 125 were demonstrated to be independent prognosticators for the survival of PMP patients. CA 19-9 can assist in judging the proliferative activity of cancer cells; one former study found that CA 19-9 may play a potential role in mediating tumor cell adhesion and disease progression in PMP, while other studies have confirmed that CA 19-9 could serve as an independent prognostic factor for predicting survival in PMP. CA 125 can predict ovarian cancer in general practice, which is also expressed in peritoneal malignancy and can be elevated in patients with any source of peritoneal irritation. CA 125 may also help to judge the tumor burden of peritoneal carcinoma. In the present study, CA 125 seems as well to be a useful marker for prediction survival of PMP patients, with a high CA 125 level denoting a poor prognosis of PMP. While the univariate analysis revealed that elevated CEA, CA 724, and CA 242 levels were all associated with poor survival in PMP, the inclusion of these parameters in the multivariate analysis did not yield a degree of statistical significance. A former study also confirmed that CEA boasts a low value in the prediction survival of PMP patients. Due to the extremely low incidence rate of PMP, few cases were included in the present study; therefore, studies with larger sample sizes and longer follow-up times are needed to assess the predictive value of tumor markers in PMP patients.

The completeness of cytoreduction is one of the most important prognostic factors for PMP, and the present study revealed that the MTD group had an obvious reduced rate of survival relative to the CCRS group. Notably, this result is consistent with those of previous studies. However, a large proportion of participants in the former study reached CCRS, while, in our study, the majority of patients could only undergo major debulking surgery; we speculate that most PMP patients in China
| Variable                                | No. | Univariate analysis | Multivariate analysis |
|-----------------------------------------|-----|---------------------|-----------------------|
|                                        |     | HR (95% CI)         | p value               | HR (95% CI)         | p value               |
| **Factors selected**                   |     |                     |                       |                     |                       |
| d-dimer (ng/ml)                         |     |                     |                       |                     |                       |
| 0–449                                   | 55  | Ref.                | —                     | Ref.                | —                     |
| >449                                    | 91  | 3.79 (2.30–6.26)    | 0.001                 | 2.67 (1.37–5.19)    | 0.004                 |
| Data missing                            | 1   | —                   | —                     | —                   | —                     |
| Preoperative CA 125 level (U/mL)        |     |                     |                       |                     |                       |
| 0–118.90                               | 98  | Ref.                | —                     | Ref.                | —                     |
| >118.90                                 | 49  | 4.28 (2.35–7.80)    | 0.001                 | 3.52 (1.87–6.62)    | 0.001                 |
| Preoperative CA 19–9 level (U/mL)       |     |                     |                       |                     |                       |
| 0–511.23                                | 131 | Ref.                | —                     | Ref.                | —                     |
| >511.23                                 | 16  | 5.41 (1.58–18.54)   | 0.001                 | 3.13 (1.52–6.45)    | 0.002                 |
| Degree of radical surgery               |     |                     |                       |                     |                       |
| CCRS                                    | 40  | Ref.                | —                     | Ref.                | —                     |
| MTD                                     | 107 | 3.03 (1.76–5.20)    | 0.002                 | 3.80 (1.76–8.22)    | 0.001                 |
| Histological grade                      |     |                     |                       |                     |                       |
| DPAM                                    | 115 | Ref.                | —                     | Ref.                | —                     |
| PMCA                                    | 17  | 3.67 (1.52–8.85)    | 0.001                 | 2.04 (1.04–3.99)    | 0.037                 |
| PMCA-S                                  | 15  | 4.28 (1.49–12.28)   | 0.001                 | 3.57 (1.70–7.48)    | 0.001                 |
| Factors not selected                    |     |                     |                       |                     |                       |
| Sex                                     |     |                     |                       |                     |                       |
| Women                                   | 49  | Ref.                | —                     | —                   | —                     |
| Men                                     | 98  | 1.73 (1.03–2.92)    | 0.059                 | —                   | —                     |
| Age (years)                             |     |                     |                       |                     |                       |
| 0–45                                    | 19  | Ref.                | —                     | —                   | —                     |
| >45                                     | 128 | 1.59 (0.78–3.22)    | 0.273                 | —                   | —                     |
| Chemotherapy before CRS                 |     |                     |                       |                     |                       |
| No                                      | 135 | Ref.                | —                     | —                   | —                     |
| Yes                                     | 12  | 2.09 (0.81–5.36)    | 0.036                 | —                   | —                     |
| Barthel Index Score (points)            |     |                     |                       |                     |                       |
| >80                                     | 125 | Ref.                | —                     | —                   | —                     |
| 0–80                                    | 15  | 2.39 (0.93–6.15)    | 0.009                 | —                   | —                     |
| Data missing                            | 7   | —                   | —                     | —                   | —                     |
| Albumin (g/L)                           |     |                     |                       |                     |                       |
| >33.1                                   | 105 | Ref.                | —                     | —                   | —                     |
| 0–33.1                                  | 42  | 2.16 (1.18–3.96)    | 0.003                 | —                   | —                     |
| Hemoglobin (g/L)                        |     |                     |                       |                     |                       |
| >120                                    | 67  | Ref.                | —                     | —                   | —                     |
| 0–120                                   | 80  | 1.63 (0.99–2.70)    | 0.057                 | —                   | —                     |
cannot obtain a correct PMP diagnosis in a timely manner. Tumor burden is a prognostic factor for predicting OS of cancer patients, where the extent of the disease in PMP is assessed by the PCI, and a score of at least 20 points always represents unresectable disease. Former studies have confirmed that PCI is a risk factor for postoperative morbidity in univariate analysis; however, no statistically significant correlation was found during the multivariate analysis. The present study also found that PCI was not an independent prognostic factor for survival prediction in PMP. In clinical practice, we found that some patients with high tumor loads can also achieve CCRS; therefore, the degree of surgery may boast a higher predictive value for prognosis than that of PCI in PMP patients.

Some researchers reckon that the prognosis of PMP correlates closely with histopathological classification. By contrast, others have suggested that PMP is unlike other tumors, and histopathology does not reliably predict tumor behavior. The present study revealed that histological grade is an independent prognostic factor for PMP patients,

Table 2 (Continued)

| Variable                  | No. | Univariate analysis | Multivariate analysis |
|---------------------------|-----|---------------------|-----------------------|
|                           |     | HR (95% CI)         | p value               | HR (95% CI)         | p value               |
| Preoperative CEA level (ng/mL) |     |                     |                       |                     |                       |
| 0–13.34                   | 47  | Ref.                | —                     | —                   | —                     |
| >13.34                    | 100 | 2.70 (1.60–4.53)    | 0.001                 | —                   | —                     |
| Preoperative CA 724 level (U/mL) |     |                     |                       |                     |                       |
| 0–47.12                   | 60  | Ref.                | —                     | —                   | —                     |
| >47.12                    | 85  | 2.14 (1.29–3.54)    | 0.006                 | —                   | —                     |
| Data missing              | 2   | —                   | —                     | —                   | —                     |
| Preoperative CA 242 level (kU/L) |     |                     |                       |                     |                       |
| 0–12.90                   | 24  | Ref.                | —                     | —                   | —                     |
| >12.90                    | 117 | 3.24 (1.77–5.91)    | 0.007                 | —                   | —                     |
| Data missing              | 6   | —                   | —                     | —                   | —                     |
| PCI                       |     |                     |                       |                     |                       |
| 0–34                      | 117 | Ref.                | —                     | —                   | —                     |
| >34                       | 30  | 2.73 (1.24–5.99)    | 0.001                 | —                   | —                     |

Abbreviations: CCRS, complete cytoreduction surgery; DPAM, disseminated peritoneal adenomucinosis; MTD, maximal tumor debulking; PMP, pseudomyxoma peritonei; PCI, peritoneal carcinomatosis index; PMCA, peritoneal mucinous carcinomatosis; PMCA-S, peritoneal mucinous carcinomatosis with signet ring cells.

Figure 3: Nomogram to predict 1-, 2-, and 3-year OS rates of pseudomyxoma peritonei patients.
where a high histological grade suggests poor survival. The different conclusions may be related to the change of criteria on histological grade; in the former study, the appendiceal pathology was classified as either low- or high-grade adenocarcinoma, while, in our research, the histological grade was divided into four subtypes according to the PSOGI criteria, which were established in 2016. We think that histological grading is of certain guiding significance for the prognosis of PMP patients.

A contradictory conclusion seems to exist in the present study. In the univariate analysis, the survival rate of PMP patients with preoperative systemic chemotherapy appeared lower than that of patients without preoperative systemic chemotherapy. Further analysis found that this may be due to bias in the selection of patients for preoperative systemic chemotherapy, as the PCI values of the 12 patients who received preoperative systemic chemotherapy were significantly higher than those of patients who did not receive preoperative systemic chemotherapy (33 [29–36] vs. 27 [22–33]; Z = −2.062; p = .039). Physicians at our center often choose patients with a heavy tumor burden to undergo preoperative systemic chemotherapy, and patients with a heavy tumor burden often have a poorer prognosis; therefore, this seemingly contradictory phenomenon was also found in the present study.

There were several limitations to the present study. First, due to the limitations of a retrospective study design, records of some data in the database were missed. Second, the predictive accuracy and discriminative ability of the established nomogram in the present study only underwent internal validation; an external validation assessment with a separate cohort remains to be undertaken in future. Finally, some other prognostic factors were not included in the prediction model, such as KRAS mutations, which have been proven to be independently prognostic for progression-free survival in PMP patients.12 Future work will further verify this hypothesis.

5 CONCLUSION

To conclude, the present study comprehensively identified five independent prognostic factors for PMP patients, including D-dimer, CA 125, CA 19-9, degree of radical surgery, and histological grade. Based on these variables, the established nomogram possesses a reasonable degree of prediction performance, and we could calculate an accurate individual survival probability. More research is needed to verify and improve the prediction model, particularly prospective large-sample studies for external validation.

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CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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