

ANALYSIS

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# Comprehensive conditional survival analysis of pancreatic signet ring cell carcinoma: chemotherapy's role and predictive model development using the SEER database

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## Abstract

**Background** Pancreatic signet ring cell carcinoma (PSRCC) is a rare and aggressive subtype of pancreatic cancer, with a poor prognosis and limited evidence on the survival benefit of chemotherapy. From the perspective of conditional survival (CS) prognosis, this study sought to assess the effect of chemotherapy on PSRCC survival and to construct a predictive model integrating CS analysis.

**Methods** Using the SEER database, 708 PSRCC patients diagnosed between 2000 and 2019 were analyzed. Propensity score matching (PSM) and Kaplan-Meier curves were employed to assess chemotherapy's impact on survival. The CS analysis was performed to evaluate dynamic survival probabilities. A nomogram was developed based on key prognostic factors identified through random survival forests (RSF), least absolute shrinkage and selection operator (LASSO) regression, and multivariate Cox analysis with a stepwise backward elimination procedure. And multiple evaluation methods were employed to assess the performance of the nomogram.

**Results** The CS analysis for all cohort showed a rapid decline in survival probability within the first few years, dropping to 18% by year 1, 5% by year 3 and 3% by year 5. Chemotherapy improved short-term survival, with a 30% one-year survival rate compared to 8% in the non-chemotherapy group. However, long-term survival probabilities converged after the first year. Key prognostic factors included age, tumor size, stage, site, surgery, and chemotherapy were identified to develop a CS-integrated nomogram. And the nomogram was found to have strong predictive accuracy and clinical utility, validated by calibration, ROC, and decision curve analyses.

**Conclusion** Chemotherapy offered significant early survival benefits in PSRCC, although its long-term impact is limited. The developed nomogram provided a reliable tool for personalized survival prediction, with further validation needed in prospective studies.

**Keywords** Pancreatic signet ring cell carcinoma, SEER, Chemotherapy, Conditional survival, Nomogram



## 1 Introduction

Pancreatic signet ring cell carcinoma (PSRCC) is a rare and aggressive subtype of pancreatic adenocarcinoma, accounting for less than 1% of pancreatic cancers [1–3]. It is characterized by the presence of signet ring-shaped cells, where the nucleus is displaced to the periphery due to large intra-cytoplasmic mucin vacuoles, which comprise over 50% of the cell's mucin content [4]. Clinically, PSRCC presents with non-specific symptoms similar to other pancreatic cancers, such as abdominal pain, jaundice, and weight loss, often leading to late diagnosis [2]. While surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapies are available for treating pancreatic cancer, their effectiveness is often limited [5, 6]; and the rarity of PSRCC also significantly hinders the development of its standardized therapeutic guidelines. Prognosis is exceedingly poor, with most patients having advanced disease at diagnosis, leading to a 5-year survival of 11.5% [7]. The rarity and poor prognosis of PSRCC underscore the need for focused research to improve understanding of its prognosis and therapeutic responses.

The treatment of PSRCC follows a similar approach to pancreatic adenocarcinoma, where surgery remains the only potentially curative option. However, due to the high rates of metastasis and recurrence, surgery is feasible in only a minority of patients [8]. Chemotherapy, either as an adjuvant or palliative treatment, has been utilized to improve survival outcomes [1, 8, 9]. However, the survival benefit of chemotherapy in PSRCC remains largely unvalidated [3, 7], owing to the rarity of the disease and the consequent lack of large cohort studies. Given these uncertainties, there is a pressing need for studies like ours to analyze the role of chemotherapy in improving survival outcomes, using propensity score matching (PSM) to mitigate selection bias and provide a more robust assessment of chemotherapy's efficacy.

PSRCC is characterized by an extremely poor prognosis, with a substantial proportion of patients succumbing to the disease within the first year following diagnosis. Traditional survival analysis techniques, while useful, do not account for the dynamic changes in survival probability over time, particularly in patients who have already survived for a certain period [10, 11]. In contrast, conditional survival (CS) analysis offers a more refined approach, enabling the evaluation of survival probabilities at different time points after diagnosis [10, 12–14]. This allows for a clearer understanding of when the mortality risk is highest, and how survival prospects evolve for patients who survive beyond critical time points. Given the aggressive nature of PSRCC, CS analysis provides a valuable tool for understanding long-term outcomes, guiding both patient counseling and treatment decisions [10, 12, 15]. Additionally, the incorporation of such dynamic survival data into predictive tools, such as nomograms, can offer clinicians a more personalized method for estimating patient survival over time.

Therefore, in this study, we employed the SEER database to conduct an in-depth analysis of PSRCCs, focusing on the survival benefit of chemotherapy through PSM analysis. Additionally, we utilized CS analysis to capture the dynamic survival patterns over different time periods after diagnosis, and developed a nomogram based on this analysis to aid in personalized survival prediction.

## 2 Methods

### 2.1 Study population

The SEER-17 Regs Research Plus Data was accessed through SEER\*Stat software version 8.4.3 (<https://seer.cancer.gov/seerstat/software/>) from the National Cancer Institute, NIH, USA. Patients were included in the study if they had a primary tumor identified in the 'Pancreas' with International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) code '8490/3: signet ring cell carcinoma.' The analysis focused on cases diagnosed from 2000 to 2019. Due to the rarity of this type of tumor, efforts were made to maximize the sample size while ensuring sufficient follow-up time to support the effective implementation of CS analysis. Patients were excluded if any information was missing, such as records for surgery, survival status, or time. Ultimately, 708 patients were included in the study.

### 2.2 Variables

The following variables were obtained from the SEER database: age at diagnosis, sex, marital status, race, tumor size, primary tumor site, SEER summary stage, tumor grade, type of primary surgery, radiation treatment, chemotherapy, presence of liver metastasis, vital status, and survival duration. Primary sites were categorized into "Head," "Body/Tail," and "Others/Not Otherwise Specified (NOS)." Staging information was derived from the SEER Summary Stage 2000, which classifies disease extent as either "localized/regional" or "distant." Localized/regional disease refers to tumors confined to the pancreas, while regional disease includes tumors extending to adjacent organs, regional lymph nodes, or both. Distant disease is defined as cases with metastases present at diagnosis [3]. Survival months were defined as the duration from the month of initial diagnosis to either the patient's death from any cause or the last month of follow-up.

### 2.3 Outcomes

The primary outcome was overall survival (OS), which refers to death from any cause, along with the CS, derived from OS. CS rate indicates the probability that a patient will survive for an additional period, given that they have already lived for a specific duration [16, 17]. For instance, if a patient has survived for 2 years, the CS rate assesses the likelihood of survival from that 2-year point onward. This measure offers a more precise insight into a patient's prognosis, especially for long-term survivors.

### 2.4 Statistics analysis

We began by performing descriptive statistics for the entire cohort, presenting categorical variables as percentages. Following this initial analysis, we investigated the 5-year CS outcomes for these patients, providing insights into long-term patient prognoses. All statistical analysis were conducted using R software (version 4.2.3, <http://www.r-project.org>). A two-sided p-value of less than 0.05 was considered statistically significant.

### 2.5 Propensity score matching analysis

Due to the unclear effects of chemotherapy on this type of tumor, we compared the prognostic probabilities between the chemotherapy group and the non-chemotherapy group from the perspective of CS analysis. To further strengthen the reliability and validity of our conclusions, we employed propensity score matching (PSM). This method enabled

us to create a balanced 1:1 match between the chemotherapy and non-chemotherapy groups, thereby controlling for potential confounding variables [18]. For PSM, we evaluated covariate balance by plotting the distribution of covariates in each group before and after matching using histograms plots. By comparing the distributions of covariates in the two groups before and after matching, if the distributions become more consistent after matching, it indicates that the matching process was effective. Subsequently, we utilized Kaplan-Meier curve analysis on the matched data to validate the advantages of chemotherapy, offering a robust assessment of its impact on patient survival outcomes. This comprehensive approach ensures a thorough evaluation of treatment efficacy in our study.

## 2.6 Model development and validation

Next, we aimed to develop a nomogram model that incorporates CS analysis. To begin, the entire cohort was randomly divided into a training group and a validation group in a 7:3 ratio. We then employed the random survival forests (RSF) algorithm and the least absolute shrinkage and selection operator (LASSO) regression for variable selection within the training cohort [19]. The variables identified through these methods were subsequently assessed using a multivariate Cox regression model, employing a stepwise backward elimination process to refine and optimize the final set of variables. The final selection of model variables was based on the Akaike Information Criterion (AIC) for evaluation. This statistical measure balances goodness-of-fit with model complexity, facilitating the identification of the most appropriate model. A smaller AIC value indicates a superior model. Finally, we developed a nomogram model utilizing the selected prognostic variables to predict CS probabilities. This model provided a visual representation of the relationship between the factors and survival outcomes while also accounting for the duration of patient survival, enabling clinicians to estimate individual prognoses more accurately.

To further validate the superior performance of our model, we utilized several metrics, including the concordance index (C-index), calibration curves, receiver operating characteristic (ROC) curves, and decision curve analysis (DCA). These evaluations were conducted on both the training and validation cohorts, providing a comprehensive assessment of the model's predictive accuracy and clinical applicability. By employing these statistical tools, we aimed to ensure the robustness and reliability of our results.

## 3 Results

### 3.1 Demographic and clinical characteristics

A total of 708 patients who met the study criteria were included in the analysis, with 495 patients assigned to the training group and 213 to the validation group. Among these patients, 517 (73%) were aged over 60 years. Gender distribution revealed that 306 patients (43.2%) were female, while 585 patients (82.6%) identified as White. Tumor locations were classified as follows: 338 patients (47.7%) had tumors located in the head of the pancreas, whereas 166 patients (23.4%) had tumors situated in the body or tail. Surgical intervention was performed in 589 patients (83.2%), in contrast, only 90 patients (12.7%) received radiation therapy, and 324 patients (45.8%) underwent chemotherapy. The demographic details and tumor characteristics are summarized in Table 1.

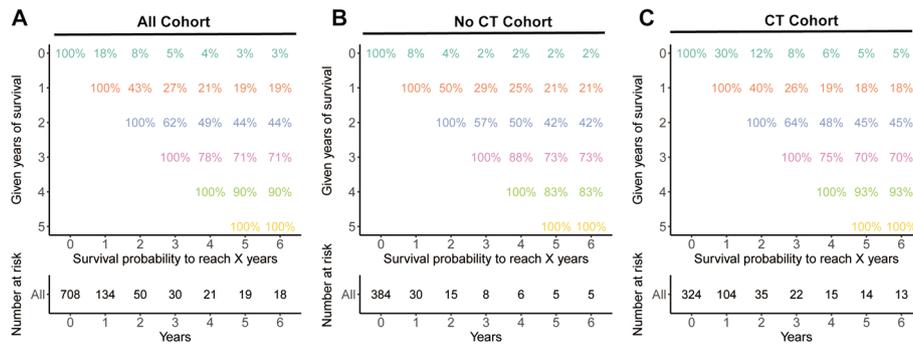
**Table 1** Baseline characteristics of patients with PSRCC

	Overall (N= 708)	Training (N= 495)	Validation (N= 213)
Age, y			
≤ 60	191 (27.0%)	129 (26.1%)	62 (29.1%)
> 60	517 (73.0%)	366 (73.9%)	151 (70.9%)
Sex			
Male	402 (56.8%)	288 (58.2%)	114 (53.5%)
Female	306 (43.2%)	207 (41.8%)	99 (46.5%)
Race			
White	585 (82.6%)	410 (82.8%)	175 (82.2%)
Others	123 (17.4%)	85 (17.2%)	38 (17.8%)
Tumor site			
Head	338 (47.7%)	234 (47.3%)	104 (48.8%)
Body/Tail	166 (23.4%)	116 (23.4%)	50 (23.5%)
Others/NOS	204 (28.8%)	145 (29.3%)	59 (27.7%)
Tumor size			
≤ 40 mm	262 (37.0%)	182 (36.8%)	80 (37.6%)
> 40 mm	216 (30.5%)	147 (29.7%)	69 (32.4%)
Unknown	230 (32.5%)	166 (33.5%)	64 (30.0%)
Tumor grade			
I/II	41 (5.8%)	28 (5.7%)	13 (6.1%)
III/IV	284 (40.1%)	204 (41.2%)	80 (37.6%)
Unknown	383 (54.1%)	263 (53.1%)	120 (56.3%)
Tumor stage			
Localized/regional	217 (30.6%)	159 (32.1%)	58 (27.2%)
Distant	470 (66.4%)	323 (65.3%)	147 (69.0%)
Unknown	21 (3.0%)	13 (2.6%)	8 (3.8%)
Liver metastasis			
No	187 (26.4%)	139 (28.1%)	48 (22.5%)
Yes	137 (19.4%)	96 (19.4%)	41 (19.2%)
Unknown	384 (54.2%)	260 (52.5%)	124 (58.2%)
Surgery			
No	589 (83.2%)	407 (82.2%)	182 (85.4%)
Yes	119 (16.8%)	88 (17.8%)	31 (14.6%)
Radiotherapy			
No	618 (87.3%)	434 (87.7%)	184 (86.4%)
Yes	90 (12.7%)	61 (12.3%)	29 (13.6%)
Chemotherapy			
No	384 (54.2%)	270 (54.5%)	114 (53.5%)
Yes	324 (45.8%)	225 (45.5%)	99 (46.5%)
Married			
No	291 (41.1%)	207 (41.8%)	84 (39.4%)
Yes	417 (58.9%)	288 (58.2%)	129 (60.6%)
Patient income			
< 65,000\$	314 (44.4%)	218 (44.0%)	96 (45.1%)
≥ 65,000\$	394 (55.6%)	277 (56.0%)	117 (54.9%)

NOS, not other specific

### 3.2 Conditional survival analysis

The CS analysis for all cohort showed a rapid decline in survival probability within the first few years, dropping to 18% by year 1, 5% by year 3 and 3% by year 5 (Fig. 1A). However, for patients who survived the initial years, their chances of further survival improved significantly. For example, patients who survived 1 year had a 19% probability of reaching year 5, while those who survived 3 years had a 71% chance of reaching year 5.



**Fig. 1** Conditional survival outcomes of PSRCCs in entire cohort (A), chemotherapy-untreated cohort (B) and chemotherapy-treated cohort (C). PSRCC, pancreatic signet ring cell carcinoma; CT, chemotherapy

This suggested that long-term survivors had increasingly favorable survival prospects as time progresses.

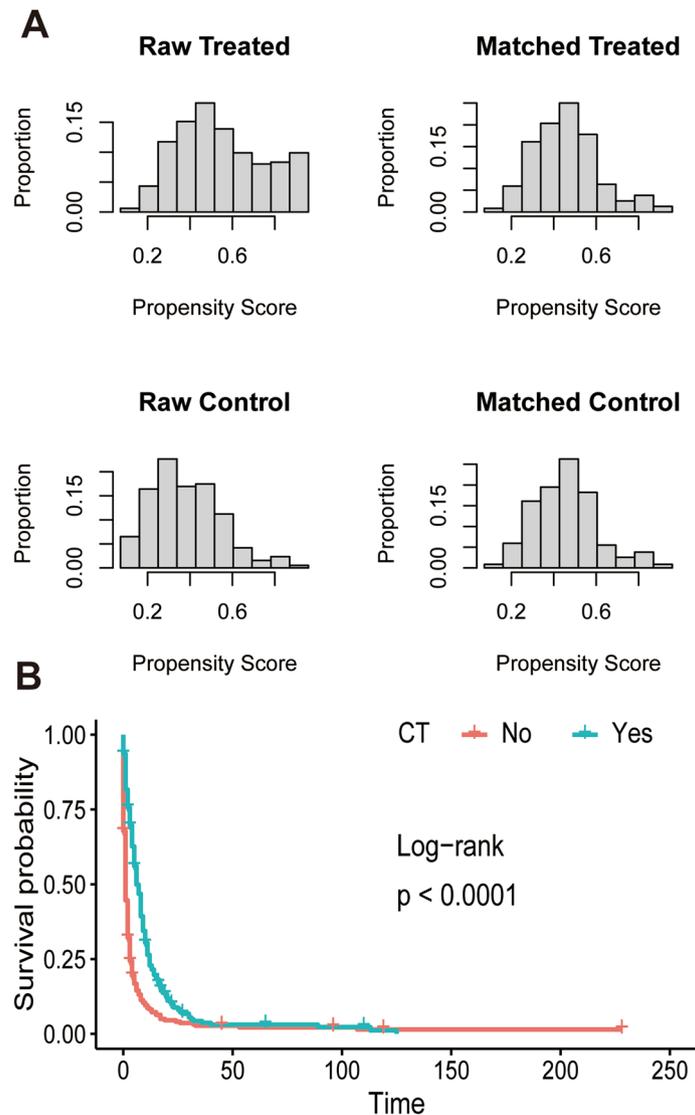
Further stratified survival analysis by chemotherapy showed that chemotherapy improved early survival, with higher probabilities of surviving the first few years (30% survival at 1 year in the chemotherapy group vs. 8% in the no chemotherapy group). However, CS analysis revealed that long-term survival probabilities converge, with both cohorts exhibiting similar survival rates after surviving the initial years following diagnosis. We also conducted a stratified CS analysis based on tumor characteristics to illustrate how various patient factors, such as age, tumor size, tumor site, and tumor stage, influence long-term survival outcomes. The results clearly demonstrated prognostic differences among these characteristics, with notably poorer CS observed in patients aged > 60 years, those with tumor size > 40 mm, and those with distant-stage tumors (Supplementary Fig. 1).

### 3.3 The survival advantage of chemotherapy use

We continued using PSM combined with Kaplan-Meier analysis to validate the survival advantage of chemotherapy. PSM analysis successfully balanced the chemotherapy treated and control groups by aligning their distributions, reducing selection bias (Fig. 2A). Further Kaplan-Meier survival curves confirmed that patients who received chemotherapy had significantly better survival outcomes compared to those who did not, with a log-rank test showing a highly significant difference ( $P < 0.05$ , Fig. 2B).

### 3.4 Conditional survival-integrated nomogram model

In this study, two advanced machine learning algorithms including the RSF and LASSO were employed to formulate prognostic models. In the RSF analysis, nine factors were identified with a mean variable importance (VIMP) greater than 0.01, including age, tumor size, tumor grade, tumor stage, tumor site, presence of liver metastasis, surgery, radiotherapy, and chemotherapy (Fig. 3A). The LASSO regression analysis revealed that key prognostic factors included age, tumor grade and size, tumor site and stage, presence of liver metastasis, as well as treatment modalities like surgery, radiotherapy, chemotherapy, and marital status (Fig. 3B). Further analysis using multivariate Cox stepwise backward regression confirmed that 7 of the 9 variables identified by the LASSO model constituted the best-fit model with the lower AIC value (AIC: RSF 4734.63; LASSO 4733.67). Finally, based on the identified optimal combination of variables, including

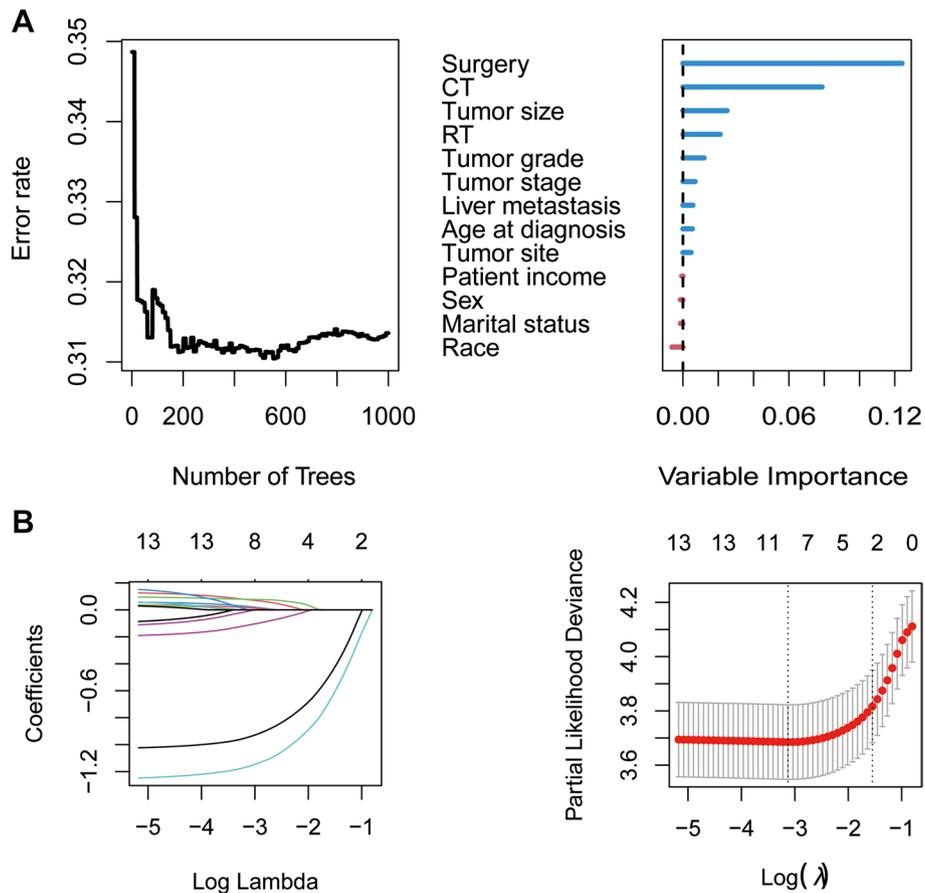


**Fig. 2** Propensity score matching analysis successfully balanced the chemotherapy treated and control groups by aligning their distributions (**A**) and Kaplan-Meier survival curves confirmed that patients who received chemotherapy had significantly better survival outcomes compared to those who did not (**B**)

age, tumor size, tumor site, tumor stage, surgery, chemotherapy, and marital status, we successfully developed a nomogram model for predicting 5-year OS and CS probabilities (Fig. 4).

### 3.5 Nomogram model test and validation

The performance of the model was evaluated using several key metrics, including the calibration curve, C-index, ROC curve, and DCA curve. The calibration curves demonstrated good consistency between the predicted and observed outcomes in both the training (Fig. 5A) and validation (Fig. 5B) sets. The C-index, which assesses the model's discriminatory power, indicated strong predictive ability, with values of 0.769 for both the training set and the validation set—values above 0.7 suggest practical utility for survival models. For the ROC curves, the AUC values for 1-, 3-, and 5-year survival predictions were 0.82, 0.87, and 0.85, respectively, in the training set (Fig. 6A), and 0.85, 0.94,



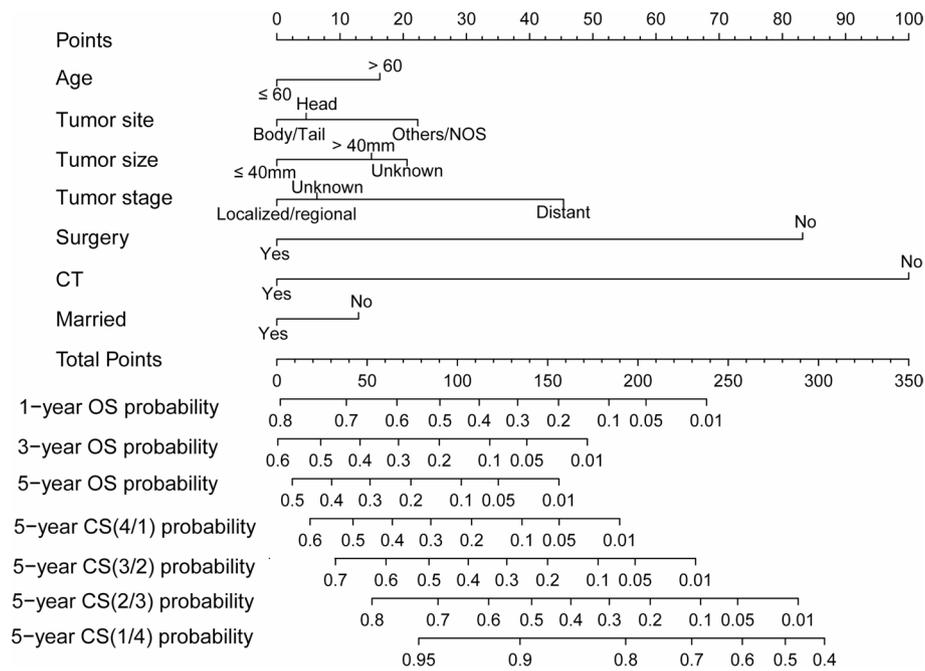
**Fig. 3** Prognostic factors selection. Random survival forests (RSF) algorithm **(A)** and the least absolute shrinkage and selection operator (LASSO) regression **(B)** for variable selection within the training cohort

and 0.95 in the validation set (Fig. 6B), indicating excellent model performance in terms of predictive accuracy. Finally, the DCA curves also demonstrated favorable clinical utility in both the training (Fig. 7A-C) and validation (Fig. 7D-F) cohorts, suggesting that the model can provide meaningful benefit in clinical decision-making.

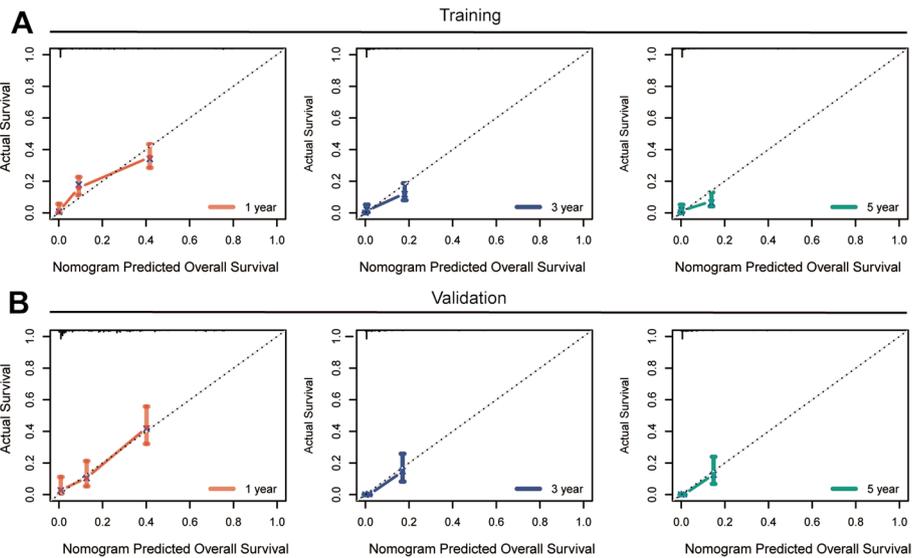
#### 4 Discussion

PSRCC is a rare and highly aggressive malignancy, with a notoriously poor prognosis [20]. Due to its rapid progression and frequent late-stage diagnosis, PSRCC patients often face limited therapeutic options and dismal survival outcomes. Chemotherapy has been widely used in pancreatic cancers [20], but its survival benefit in PSRCC remains uncertain due to a lack of comprehensive studies. Given the limited evidence, it is critical to explore the role of chemotherapy in this rare subtype and analyze survival trends to guide treatment decisions. This study sought to investigate the survival benefits of chemotherapy and develop a predictive nomogram model to provide more accurate prognostic insights. Our findings showed that chemotherapy offered short-term survival benefits, particularly in the first year after diagnosis, while long-term survival advantages remained modest. Additionally, we identified key prognostic factors for CS-integrated nomogram establishment.

Our analysis revealed that the mortality rate for PSRCC is exceptionally high within the first year of diagnosis, but patients who survived beyond this critical period showed

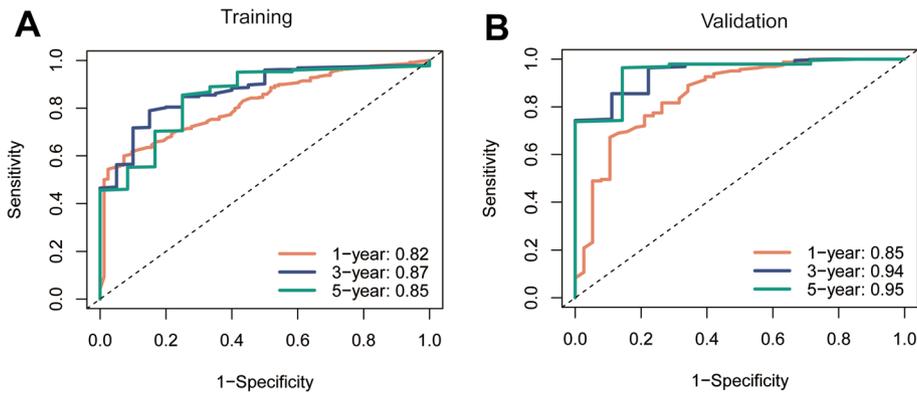


**Fig. 4** Conditional survival integrated nomogram model was established for predicting 5-year overall survival and conditional survival probabilities of PSRCC patients. PSRCC, pancreatic signet ring cell carcinoma

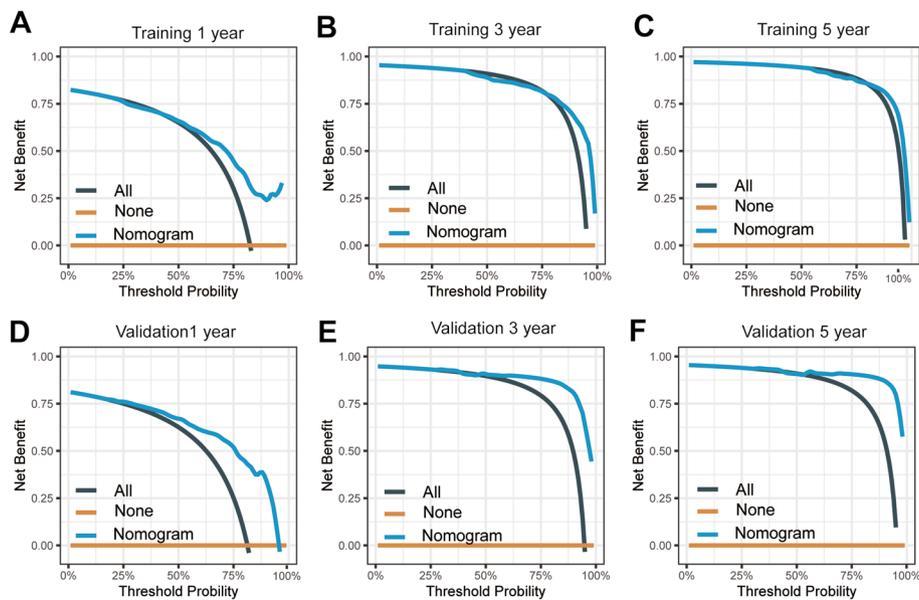


**Fig. 5** The calibration curves demonstrated good consistency between the predicted and observed outcomes in both the training (A) and validation (B) sets

a significant improvement in their 5-year CS probability. This finding had important clinical implications, as it underscored the need for intensive monitoring and treatment in the early stages post-diagnosis. CS analysis, unlike traditional methods, provides dynamic updates on survival probabilities over time, allowing clinicians to adjust prognostic expectations as patients surpass early mortality risks [16]. The increase in 5-year CS probability after the first year indicated that if patients can overcome the early high-risk phase, their chances of longer-term survival improved substantially. This result



**Fig. 6** The ROC curves showing AUC values for 1-, 3-, and 5-year survival predictions: 0.82, 0.87, and 0.85, respectively, in the training set (A), and 0.85, 0.94, and 0.95 in the validation set (B). ROC: Receiver operating characteristic; AUC: Area under the curve



**Fig. 7** DCA curves demonstrating favorable clinical utility in both the training (A-C) and validation (D-F) cohorts, indicating that the model offers meaningful benefit for clinical decision-making. DCA: Decision curve analysis

highlighted the importance of targeted interventions during the critical first year to improve patient outcomes.

The current treatment landscape for PSRCC is limited, with chemotherapy being the primary systemic therapy. However, its role in improving outcomes of PSRCCs is needed to be further validated. Huang et al. also reported the beneficial effects of chemotherapy on OS and cancer-specific survival in patients with PSRCC and recommended it in clinical practice [7]. Radojkovic et al. reported a PSRCC patient who responded well to a 3-month course of neoadjuvant chemotherapy with gemcitabine, with the tumor in the pancreas shrinking from 4.5 cm to 1.5 cm in diameter [9]. Our PSM analysis with survival analysis compared the outcomes between chemotherapy-treated and untreated patients. The results demonstrated that chemotherapy significantly improved short-term survival, especially within the first year, as indicated by the improved survival rates. However, its impact on long-term survival was limited, suggesting that while chemotherapy

is beneficial in extending early survival, its effectiveness diminishes over time due to the chemotherapy resistance. Pancreatic cancer resists therapy through a complex and adaptive tumor microenvironment. Poor blood supply limits drug delivery while inducing hypoxia-driven autophagy and metabolic reprogramming, which help cancer cells evade the immune system by degrading MHC-I [21–23]. Meanwhile, a dense fibrotic stroma, shaped by different cancer-associated fibroblast (CAF) subsets (e.g.,  $\alpha$ -SMA<sup>+</sup> vs. FAP<sup>+</sup> CAFs), creates physical barriers and suppresses immune responses. Pancreatic cancer's "cold tumor" nature—marked by low neoantigen levels, exclusion of cytotoxic T cells, and infiltration of immunosuppressive cells—further weakens immune attack [21–23]. The microenvironment's plasticity enables rapid adaptation through metabolic shifts (e.g., autophagy vs. macropinocytosis) and KRAS pathway rewiring, fostering cooperation between cancer and stromal cells [21, 22]. Additionally, the tumor's heterogeneity, both in cancer clones and stromal organization, creates evolutionary pressure that undermines single-target therapies [23, 24]. Moreover, despite high mutational burdens in non-microsatellite instability-high cases, immunotherapy remains ineffective, and combination strategies targeting immune-resistance mechanisms, including mutant KRAS, are needed [23–25]. Future research should focus on identifying key adaptive mechanisms, developing precision-targeted therapies, and leveraging spatial multi-omics to map tumor-stroma interactions. Advancing personalized treatment strategies based on tumor heterogeneity and microenvironmental dynamics will be crucial in improving pancreatic cancer outcomes. These findings further reinforced the need for multimodal treatment strategies that go beyond chemotherapy to achieve durable long-term outcomes.

We then applied rigorous statistical methods, including RSF and LASSO regression, to identify optimal combination of prognostic factors for PSRCC. Finally, we determined that age, tumor size, tumor site, tumor stage, surgery, chemotherapy, and marital status constituted the best combination of predictors for survival in our study. These factors were used to develop a nomogram that integrated CS probabilities, offering a practical tool for clinicians to estimate patient survival dynamically. The model's performance, validated through calibration curves, ROC, and DCA analyses, demonstrated excellent predictive accuracy in both the training and validation cohorts. To use the nomogram, clinicians first identify key variables, then assign each variable a corresponding point score. Summing these scores yields a total score, which is mapped to a probability scale to determine CS. This improved prognosis may justify reducing follow-up intensity or adjusting treatment strategies. Conversely, if CS remains poor, continued aggressive therapy or clinical trial enrollment may be considered. By integrating real-time survival probabilities, the nomogram enhances personalized decision-making, optimizing surveillance, treatment, and patient counseling based on evolving risk assessments.

Several limitations must be acknowledged in our study. The use of the SEER database, while comprehensive, presents certain drawbacks, including a lack of information on treatment regimens, tumor recurrence status, detailed comorbidities, medication histories, and genetic data, all of which could influence survival outcomes. And missing data for key variables such as tumor size, staging, and tumor grade could impact the accuracy of our analysis and the interpretation of results. While the SEER database lacks granular details on chemotherapy regimens (e.g., drug types, doses, duration), our PSM analysis focused on evaluating the overall survival benefit of chemotherapy as a binary variable

(administered vs. not administered). Additionally, as a retrospective analysis, inherent biases and unmeasured confounding variables may have affected the results [26]. Moreover, that the SEER data primarily reflect the American population and may not fully represent patients from other regions. And the rarity of PSRCC limits the generalizability of our findings to broader populations, and prospective studies with larger sample sizes from international cohorts are needed to confirm these results. Finally, while our nomogram showed excellent predictive accuracy, external validation in independent datasets would further strengthen its clinical applicability. Despite these limitations, the SEER database remains a valuable resource, particularly for rare tumors, as it provides a large sample size and long-term follow-up data that would be difficult to obtain from single-center or smaller cohort studies. These advantages enable more comprehensive survival analyses and improve our understanding of disease progression over time.

## 5 Conclusion

In this comprehensive study of PSRCC using the SEER database, we provided valuable insights into the CS patterns of this rare and aggressive malignancy. Our analysis demonstrated that chemotherapy improved short-term survival, particularly in the first year after diagnosis, though its long-term impact remains limited. CS analysis revealed that patients who survived beyond the critical first year had significantly improved survival prospects, underscoring the importance of early intervention. The development of a CS-based nomogram offered clinicians a robust tool for individualized survival prediction.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1007/s12672-025-02946-w>.

Supplementary Material 1

### Author contributions

MY and ZZ designed the study and analyzed the data. MY, CX and ZZ did the statistical analysis and wrote the main manuscript text. MY prepared all figures. YM and ZZ revised the manuscript. All authors reviewed the manuscript and agreed to the published version of the manuscript.

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None.

### Data availability

The data are available from the National Cancer Institute's Surveillance, Epidemiology, and End Results database at: <https://seer.cancer.gov/>.

## Declarations

### Human ethics and consent to participate

Not applicable.

### Competing interests

The authors declare no competing interests.

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