Objective: We aimed to develop a nomogram to predict the survival and prognosis of adenosquamous carcinoma of the pancreas (ASCP).

Background: Adenosquamous carcinoma of the pancreas (ASCP) is a relatively rare histological subtype of pancreatic exocrine neoplasms. It was reported a worse survival in ASCP than in pancreatic adenocarcinoma (PDAC). Prediction of ASCP prognosis is of great importance.

Methods: Histologically confirmed ASCP patients from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program database were finally enrolled and divided into development and internal validation cohorts. Moreover, a multi-center cohort of 70 patients from China was registered as the external validation. A nomogram was developed based on independent predictors of ASCP determined in multivariable analysis.

Results: A total of 233 patients from SEER were finally included. Univariate and Multivariate analysis showed that tumor size, radiotherapy, chemotherapy, and lymph node ratio (LNR) were considered the independent prognostic indicators. We developed a nomogram according to these four parameters. The C index of the nomogram in the development cohort was 0.696. Through analysis of the area under the curve (AUC) of the different cohorts, we observed that the predictive efficacy of the nomogram for 1-, and 2-year overall survival (OS) were better than those of the American Joint Committee on Cancer (AJCC) TNM (8th) staging system both in the development and validation.
cohort. External validation confirmed that 1-year survival is 67.2% vs. 29.7%, similar to the internal cohort analysis.

**Conclusion:** The nomogram showed good performance in predicting the survival of ASCP. It could help surgeons to make clinical decisions and develop further plans.

**KEYWORDS**
adenosquamous carcinoma, pancreas, nomogram, prognosis, the TNM 8th staging system

**Highlights**
- We developed a nomogram especially for adenosquamous carcinoma of the pancreas (ASCP) to predict the survival and prognosis.
- Univariate and multivariate analysis showed that four parameters, including tumor size, radiotherapy, chemotherapy, and lymph node ratio (LNR), could influence the survival of ASCP patients.
- In addition, by comparing the nomogram’s efficiency with AJCC TNM (8th) staging system, it was proved that the nomogram is superior to the TNM stage in predicting the prognosis.
- Finally, we applied the external cohort from multi-center to verify the performance and get satisfactory results. Our nomogram has clinical applicability.

**Methods**

**Patient and date collection**

The SEER database (2004–2016) was used to identify the ASCP patients. Patients were retrieved based on the International Classification of Disease for Oncology (ICD, 3rd edition) codes for pancreas tumours. In order to identify all eligible cases, the following criteria were applied: (i) all patients were diagnosed as ASCP (ICD-O-3: 8560/3) with surgical resection and pathology verified. (ii) active follow-up of patients (diagnosis not obtained from autopsy or death certificate) (iii) positive histology confirmation and surgical resection (iv) Complete data of tumor size, lymph nodes examined, and positive lymph nodes.

Two Chinese centers provided external validation data on adenosquamous carcinoma of the pancreas. Data from the following centers included Ruijin Hospital, Shanghai Jiaotong University (n = 52), and The First Affiliated Hospital of Xi’an Jiaotong University (n = 18). Electronic datasheets were provided to the two centers. The Institutional Review Boards...
of the First Affiliated Hospital of Xi’an Jiaotong University approved all the ethical information (XJTU1AF2021LSK-053).

Variables included

In the study, the following characteristics were reviewed: age, race, sex, tumor location, grade, AJCC TNM (8th) staging, T classification, N classification, M classification, radiotherapy, chemotherapy, number of lymph nodes examined, lymph nodes positive, tumor size, lymph node ratio (LNR), survival months, and vital status. The LNR is defined as the ratio of the number of metastatic lymph nodes relative to the total number of LNs examined (TNLE). The receiver-operating characteristic curve (ROC) analysis was used to investigate the discriminatory power relative to overall survival among patients who had 1 to 3 lymph node metastasis (LNM) and patients who had \( \geq 4 \) LNM.

Statistical analysis

All statistical analyses were performed by SPSS 25.0 statistical package (IBM Corporation, Armonk, NY, USA). The optimal cutoff value of the lymph nodes ratio and other parameters were analyzed by X-tile software. Continuous data were expressed in medians with interquartile range (IQR), and Mann–Whitney U tests were used to comparing these data. Categorical data were compared using \( \chi^2 \) or Fisher exact tests. The overall survival (OS) was compared by Kaplan–Meier curves and analyzed using the log-rank test via SPSS and GraphPad Prism 8.0 Software (GraphPad Software Inc. San Diego, CA, USA). The Cox proportional hazards regression models were performed to find the independent prognostic factors. The cutoff values of the variables were determined by X-tile software (Yale University, New Haven, CT, USA) (8). The resulting hazard ratios (HR) and 95% confidence interval (CI) were presented. All tests were two-sided, and \( P \)-value < 0.05 was considered statistically significant.

Nomogram establishment

We divided the whole cohort from SEER into development and internal validation cohorts at a ratio of 7:3 using a table of random numbers. Based on the results of multivariate Cox regression in the development cohort, potential risk factors (\( P < 0.05 \)) were used to establish a nomogram using the “rms” R package. The accuracy and calibration of the model were verified using the bootstrap verification method and consistency index (C-index). The closer the C-index to 1, the better the model discrimination. The closer the calibration curve of the graph calibration method is to the standard curve (slope 1), the better the predictive ability of the nomogram is. The R language software version used for the study was version 3.5.1. Additionally, we applied a multi-center cohort from China as the external cohort to confirm nomogram efficiency. The authors have completed the STROBE Statement of cohort studies checklist (9).

Results

Clinicopathological characteristics

According to the criteria above, 233 patients with histologically confirmed pancreatic adenosquamous carcinoma from the SEER database were finally included (Supplement Figure 1). There were 115 males and 118 females, with a median age of 68 (60–74). Tumors were located at the pancreatic head (116/233, 49.79%) and the body or tail (91/233, 39.06%). 56 patients (56/233, 24.03%) received radiotherapy, while 149 (149/233, 63.95%) received chemotherapy. The median number of examined lymph nodes was 15 (9–22), and the median number of tumor size was 40 (30–55) mm. A development set of SEER database (n=165) and validation set (n=68) were analyzed. The detailed baseline characteristics are displayed in Tables 1, 2.

The optimal cutoff value of the lymph nodes ratio analyzed by X-tile software was 0.18 (Supplement Figure 2). Receiver-operating characteristic (ROC) analysis illustrates that the total number of lymph nodes examined (TNLE) \( \geq 16 \) had the highest discriminatory power relative to overall survival among patients who had 1 to 3 lymph node metastasis (LNM) and patients who had \( \geq 4 \) LNM (10, 11) (AUC 0.775, Youden index 0.434, sensitivity 80.5%, specificity 62.9%, \( P < 0.001 \))(Supplement Figure 3). Above all, we choose 16 as the cutoff value of the number of lymph nodes examined.

In addition, 70 patients from the two centers in China were also included, as Table 1 shows. There were 46 males and 24 females were diagnosed with ASPC from 2012 to 2019. The median age at diagnosis was 61 (53–70). The tumor was located at the pancreatic head (n = 43) and pancreatic body or tail (n = 27). The median number of examined lymph nodes was 12 (6–18), and the median number of tumor size was 40 (30–60) mm. All the patients did not receive radiotherapy, while 34 patients received chemotherapy.

Univariate and multivariate analysis on independent prognostic factors for the prognosis of ASCP from SEER

To further analyze clinical characteristics of the survival and prognosis of patients with pancreatic adenosquamous carcinoma, we firstly conducted univariate and multivariate
analyses of the overall survival (OS) of patients with ASCP from the SEER database. A total of 233 patients were analyzed with the single-factor Cox regression. According to the results, age, tumor size, AJCC stage, N stage, chemotherapy, radiotherapy, and LNR were all related to the prognosis of patients with ASCP ($P < 0.05$) (Table 3).

According to the results of single factor analysis and professional conclusions, Cox proportional risk regression analysis was further conducted. As showed in Table 4, multivariate analysis indicated that tumor size ($P = 0.004$, HR = 1.573, 95% CI: 1.156 to 2.240), radiotherapy ($P = 0.016$, HR = 0.617, 95% CI: 0.416 to 0.914), chemotherapy ($P < 0.001$, HR = 0.511, 95% CI: 0.373 to 0.700), and LNR ($P = 0.019$, HR = 1.488, 95% CI: 1.068 to 2.074) were considered independent prognostic indicators for OS of patients with ASCP after surgical resection.

Development and validation of a nomogram for predicting ASCP survival

The nomogram included all statistically significant prognostic factors in the Cox proportional hazards regression model, including radiotherapy, chemotherapy, LNR, and tumor size (Figure 1A). Its influence on prognosis determined the score of each parameter, and the survival rate of the patients was obtained by the sum of the score of four parameters. To simplify applying the model in clinical practice, we also transformed the nomogram into a web-based calculator (https://aliez2021.shinyapps.io/DynNomapp/) (Supplement Figure 4).

To verify the efficiency of the established nomogram, we applied the bootstrap method. The C index of the nomogram in predicting survival of the development cohort was 0.696 (95% CI: 0.643-0.749). The C index in the internal validation cohort was 0.696 (95% CI: 0.617-0.776). The 1-year AUC of the development and internal validation cohort was 0.750 and 0.717, compared with 0.703 and 0.717 in 2 year AUC. The development group's 1-year and 2-year calibration curves and the internal validation group did not deviate from the centerline, showing good prediction compliance (Figures 1B–E). These results showed good agreement between prediction and observation.

Comparison of the nomogram and AJCC TNM (8th) staging system

To assess the predictive value of the established nomogram, we attempted to compare the predictive efficacy with the AJCC TNM (8th) stage. Its C index in the development and internal validation cohort was 0.609 (95% CI: 0.554-0.664), 0.581 (95% CI: 0.500-0.663), respectively, inferior to the nomogram. As Figure 2 shows, through analysis of the AUC of a different cohort by ROC curves analysis, we also observed that the AUCs of the nomogram for 1-, 2- OS were better than those of the TNM stage in the development and validation cohort. (nomogram vs TNM, development

### Table 1: The clinical characteristics of the ASCP patients from SEER and a multi-center cohort.

| Characteristics | SEER database (N = 233) | Chinese centers (N = 70) | P value |
|-----------------|------------------------|-------------------------|--------|
| Diagnosed age   | 68 (60–74)             | 61 (53–70)              | < 0.001|
| Race            | NA*                    | /                       | /      |
| Black           | 22                     | /                       | /      |
| White           | 193                    | /                       | /      |
| Others          | 18                     | /                       | /      |
| Sex             | 0.016                  |                         | /      |
| Female          | 118                    | 24                      | /      |
| Male            | 115                    | 46                      | /      |
| Tumor location  | 0.010                  |                         | /      |
| Body or tail    | 91                     | 27                      | /      |
| Head            | 116                    | 43                      | /      |
| Others          | 26                     | /                       | /      |
| Grades          | NA*                    | /                       | /      |
| I+II            | 54                     | /                       | /      |
| III+IV          | 149                    | /                       | /      |
| Unknown         | 30                     | /                       | /      |
| AJCC stages (8th) | 0.212                 |                         | /      |
| I               | 55                     | 23                      | /      |
| II              | 125                    | 36                      | /      |
| III             | 53                     | 11                      | /      |
| T Stage (8th)   | 0.203                  |                         | /      |
| T1              | 11                     | 7                       | /      |
| T2              | 109                    | 33                      | /      |
| T3              | 98                     | 23                      | /      |
| T4              | 15                     | 7                       | /      |
| N Stage (8th)   | 0.049                  |                         | /      |
| N0              | 95                     | 39                      | /      |
| N1              | 97                     | 25                      | /      |
| N2              | 41                     | 6                       | /      |
| Radiotherapy    | < 0.001                |                         | /      |
| No              | 177                    | 70                      | /      |
| Yes             | 56                     | 0                       | /      |
| Chemotherapy    | 0.021                  |                         | /      |
| No              | 84                     | 36                      | /      |
| Yes             | 149                    | 34                      | /      |
| Number of examined lymph nodes | 0.012         |                         | /      |
| Tumor size      | 40 (30-55)             | 40 (30-60)              | 0.673  |
| LNR             | 0.071 (0.0-0.20)       | 0.00 (0-0.10)           | 0.011  |

*No relevant data have been collected.

ASCP, adenosquamous carcinoma of the pancreas; SEER, the National Cancer Institute’s Surveillance, Epidemiology, and End Results; AJCC, American Joint Committee on Cancer; LNR, Lymph node ratio.
cohort: 1 year, 0.750 vs 0.663; 2 year, 0.703 vs 0.626) (Figures 2A–D). The Decision Curve Analysis (DCA) also showed that compared with the AJCC TNM (8th) staging system, the predictive efficacy of the new nomogram is significantly increased and has a wide range of threshold probabilities both in the development and validation cohort (Figures 2E, F). These results indicated that the nomogram could be more beneficial in the clinical application of predicting individual survival outcomes than the AJCC TNM (8th) staging system.

Performance of the Nomogram on external verification in a multi-center cohort from China

In order to judge the clinical applicability to other populations, we calculated the total nomogram point (NTP) and got the median number of 168.4 in the development group. Then we divided the cohorts into two subgroups according to the NTP, the low-risk group (NTP < 168.4) and the high-risk group (NTP ≥ 168.4). Moreover, there were 78 patients in the low-risk group and 87 patients in the high-risk group of the development cohort. As Figure 3 shows, The Kaplan-Meier analysis showed that the low-risk group in the development cohort had a better prognosis than the high-risk group ($P < 0.01$). Similar results were also verified in the internal validation cohort.

Next, we put our multi-center cohort (n = 70) from Shanghai Ruijin Hospital and Xi’an Jiaotong University into the model. According to the NTP, we divided the cohort into low-risk and high-risk groups (n = 19) and high-risk groups (n = 51). According to the result, the median survival time in the two groups was 35 months (the low-risk group) vs. 9 months (the high-risk group). The 1-year survival is 67.2% vs. 29.7%, similar to the internal cohort analysis. It seemed that the established nomogram had an excellent performance in the external validation and could be widely suggested.

Discussion

Pancreatic cancer is the fourth leading cause of cancer-related deaths in the United States, with 60,430 new cases and 68,220 deaths estimated in 2021 (12, 13). According to 2010 WHO classification, ASCP was classified as one subtype of PDAC (14). Previous studies consistently reported the survival or therapy of ASCP. One SEER analysis (4) compared the survival following surgical resection in patients with adenosquamous carcinoma or adenocarcinoma and the biological behavior and survival of ASCP and PDAC. Another analysis (7) focused on the benefit of chemoradiotherapy in ASCP treatment. In patients who underwent surgery, ASCP had worse OS than PDAC unless there was negative lymph node status, R0 surgical resection, and receipt of chemotherapy (15). There are relatively few models available for predicting survival outcomes of patients with ASCP.

As for PDAC, the clinician often makes empirical judgments according to the patients’ characteristics, AJCC stage, TNM stage, and pathological results. There are no specific methods for ASCP, in which all the TNM and AJCC staging criteria were

| Characteristics          | Development cohorts (N = 165) | Internal validation cohorts (N = 68) |
|--------------------------|-----------------------------|---------------------------------|
| Diagnosed age            | 67 (59-73)                  | 70 (63-75)                      |
| Race                     |                             |                                 |
| Black                    | 16                          | 6                               |
| White                    | 139                         | 54                              |
| Others                   | 10                          | 8                               |
| Sex                      |                             |                                 |
| Female                   | 91                          | 27                              |
| Male                     | 74                          | 41                              |
| Tumor location           |                             |                                 |
| Body or tail             | 67                          | 24                              |
| Head                     | 79                          | 37                              |
| Others                   | 19                          | 7                               |
| Grades                   |                             |                                 |
| I+II                     | 39                          | 15                              |
| III+IV                   | 102                         | 47                              |
| Unknown                  | 24                          | 6                               |
| AJCC stages (8th)        |                             |                                 |
| I                        | 37                          | 18                              |
| II                       | 95                          | 30                              |
| III                      | 33                          | 20                              |
| T Stage (8th)            |                             |                                 |
| T1                       | 8                           | 3                               |
| T2                       | 76                          | 33                              |
| T3                       | 71                          | 27                              |
| T4                       | 10                          | 5                               |
| N Stage (8th)            |                             |                                 |
| N0                       | 69                          | 26                              |
| N1                       | 72                          | 25                              |
| N2                       | 24                          | 17                              |
| Radiotherapy             |                             |                                 |
| No                       | 119                         | 58                              |
| Yes                      | 46                          | 10                              |
| Chemotherapy             |                             |                                 |
| No                       | 59                          | 25                              |
| Yes                      | 106                         | 43                              |
| Number of examined lymph nodes |             |                                 |
| Tumor size               | 40 (30-55)                  | 40 (30-50)                     |
| LNR                      | 0.070 (0-0.185)             | 0.0070(0-0.208)                |
### TABLE 3 Univariate analysis of clinical characteristics in ASCP patients.

| Characteristics | N (%) | Univariate analysis | HR | 95% CI | P value |
|-----------------|-------|---------------------|----|--------|---------|
| Diagnosed age   |       |                     |    |        |         |
| ≤ 68            | 121 (51.9%) |                     | 1  | /      | /       |
| > 68            | 112 (48.1%) |                     | 1.366 | 1.011-1.845 | 0.042   |
| Race            |       |                     |    |        |         |
| Black           | 22 (9.4%) |                     | 1  | /      | /       |
| White           | 193 (82.8%) |                   | 0.661 | 0.404-1.081 | 0.099   |
| Others          | 18 (7.8%) |                     | 0.654 | 0.319-1.344 | 0.248   |
| Sex             |       |                     |    |        |         |
| Female          | 118 (50.6%) |                     | 1  | /      | /       |
| Male            | 115 (49.4%) |                     | 1.072 | 0.793-1.448 | 0.652   |
| Tumor location  |       |                     |    |        |         |
| Body or tail    | 91 (39.1%) |                     | 1  | /      | /       |
| Head            | 116 (49.8%) |                   | 1.182 | 0.859-1.627 | 0.305   |
| Unknown         | 26 (11.1%) |                     | 1.234 | 0.747-2.039 | 0.412   |
| Grades          |       |                     |    |        |         |
| I+II            | 54 (23.2%) |                     | 1  | /      | /       |
| III+IV          | 149 (63.9%) |                   | 1.084 | 0.753-1.560 | 0.665   |
| Unknown         | 30 (12.9%) |                     | 1.035 | 0.608-1.761 | 0.899   |
| AJCC stages (8th) |      |                     |    |        |         |
| I               | 55 (23.6%) |                     | 1  | /      | /       |
| II              | 125 (53.6%) |                   | 1.080 | 0.737-1.582 | 0.694   |
| III             | 53 (22.8%) |                     | 1.787 | 1.148-2.783 | 0.010   |
| T Stage (8th)   |       |                     |    |        |         |
| T1              | 11 (4.7%) |                     | 1  | /      | /       |
| T2              | 109 (46.8%) |                   | 0.790 | 0.380-1.639 | 0.526   |
| T3              | 98 (42.1%) |                     | 1.082 | 0.521-2.244 | 0.833   |
| T4              | 15 (6.4%) |                     | 1.521 | 0.630-3.675 | 0.351   |
| N Stage (8th)   |       |                     |    |        |         |
| N0              | 95 (40.8%) |                     | 1  | /      | /       |
| N1              | 97 (41.6%) |                     | 1.296 | 0.928-1.810 | 0.128   |
| N2              | 41 (17.6%) |                     | 1.838 | 1.208-2.796 | 0.004   |
| Radiotherapy    |       |                     |    |        |         |
| No              | 177 (76.0%) |                     | 1  | /      | /       |
| Yes             | 56 (24.0%) |                     | 0.475 | 0.330-0.686 | <0.001  |
| Chemotherapy    |       |                     |    |        |         |
| No              | 84 (36.1%) |                     | 1  | /      | /       |
| Yes             | 149 (63.9%) |                   | 0.444 | 0.329-0.600 | < 0.001 |
| Number of examined lymph nodes | | | | | |
| 1-15            | 125 (53.6%) |                     | 1  | /      | /       |
| ≥ 16            | 108 (56.4%) |                     | 1.013 | 0.749-1.370 | 0.934   |
| Tumor size      |       |                     |    |        |         |
| < 40mm          | 101 (43.3%) |                     | 1  | /      | /       |
| ≥ 40mm          | 132 (56.7%) |                     | 1.472 | 1.084-1.998 | 0.013   |
| LNR             |       |                     |    |        |         |
| < 0.18          | 170 (73.0%) |                     | 1  | /      | /       |
| ≥ 0.18          | 63 (27.0%) |                     | 1.663 | 1.202-2.301 | 0.002   |

ASCP, adenosquamous carcinoma of the pancreas; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer; LNR, Lymph node ratio.
proposed a novel nomogram that included the T classi-
Additionally, some research showed that larger tumor sizes
showed the best prognostic performance and a signi-
pancreatic cancer (23
independent prognostic factor for patients after resection of
survival in PC patients better than positive lymph nodes and an
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Data from Johns Hopkins Hospital show, in particular, bene-
fl
the best regimen to use, which are commonly used
operative treatment with chemotherapy, radiotherapy, or both
Patients affected by ASCP or SCC undergoing surgery and post-
treated with R0 resection and adjuvant treatment. Moreover,
relationship with locoregional recurrence in pancreatic cancer

AUCs of the development and validation cohort nomogram
rate of the patients more accurately. However, the C-indexes and

As to the poor prognosis of ASCP, Yuan Fang et al. (7)
discovered that T staging, M staging, and adjuvant treatment,
including chemo and radiotherapy; might be the indicator of
survival benefits after ASCP resection. Ning Pu et al. (12)
proposed a novel nomogram that included the T classification
and LNR in patients with resected pancreatic head carcinoma.
Additionally, some research showed that larger tumor sizes
showed a shorter median OS than the T stage (15, 22). In
recent years, LNR has been considered a robust predictor of
survival in PC patients better than positive lymph nodes and an
independent prognostic factor for patients after resection of
pancreatic cancer (23–25). You et al. (26) reported that LNR
showed the best prognostic performance and a significant
relationship with locoregional recurrence in pancreatic cancer
treated with R0 resection and adjuvant treatment. Moreover,
Patients affected by ASCP or SCC undergoing surgery and post-
operative treatment with chemotherapy, radiotherapy, or both
appear to benefit, even though there is no consensus regarding
the best regimen to use, which are commonly used
fluoropyrimidine-based, gemcitabine-based, or platinum-based.
Data from Johns Hopkins Hospital show, in particular, benefit
for ASCP patients treated with platinum-based chemotherapy,
with an OS of 19.1 months (27).

Using this nomogram, we may predict the future survival
rate of the patients more accurately. However, the C-indexes and
AUCs of the development and validation cohort nomogram
were more accurate than the current TNM staging in predicting
the prognosis. Further, DCA demonstrated its clear clinical
application advantages over the TNM staging system. To
further prove the efficiency of the nomogram, we applied two
Chinese centers to verify the nomogram. It is convincing that the
results of this study could be particularly helpful in predicting
post-operative survival of ASCP patients.

Overall, the nomogram is innovative and reasonable in the
following aspects. Firstly, variables like tumor size,
chemotherapy, radiotherapy, and LNR were used to develop
this nomogram. Secondly, the nomogram based on the SEER
database was able to predict the prognosis of ASCP. ROC curve
and DCA analyses of this study showed that the nomogram
could predict the OS of patients more accurately, which has
clinical applicability. The external validation of nomogram
prediction from the multi-center cohort was found to be
correct.

The limitation was also considered in our study. First,
though this retrospective study uses the SEER database and
two medical institutions, the sample of the external cohort is
small, and a multi-center prospective study is needed to increase
the number of cases further to improve the accuracy and
representativeness of the prediction model. We developed a
nomogram of adenosquamous carcinoma of the pancreas
(ASCP) based on retrospective studies of the SEER database,
which required further validation in prospective cohort and
clinical trials. In addition, this study did not include
information on the gene targets and molecular markers.
Targeting the tumor microenvironment may play an essential
role in the therapeutic strategies of PDAC and rare pancreatic
tumors (28, 29). Molecular biology, genetics, and epigenetics
provide new evaluation indicators of individual rare pancreatic
neoplasms’ potential behavior. Compared with PDAC, more and
more relevant studies of ASCP focused on the analysis of
molecular features and genetic alterations of ASCP (30, 31).
For example, Lenkiewicz E et al. (30) found that ASCP organoids
were carrying an FGFR1 fusion show sensitivity to pan FGFR
inhibitor (inigratinib), the first example of ASCP response to
targeted therapy. Above all, new biomarkers and genetic
alterations could be added to future prediction models of
ASCP to provide more accurate individual risk estimations.
Since there is limited literature related to ASCP, if possible, we
expect to distinguish the genomic and epigenomic landscape of
ASCP and identify new strategies for targeting this aggressive
subtype of pancreatic cancer. Molecular profiling of ASCP may
be appropriate to provide complete information regarding the

### Table 4 Multivariate analysis of different influencing factors in ASCP patients.

| Variables       | B value | SE value | Wald value | P value | HR    | 95% CI          |
|-----------------|---------|----------|------------|---------|-------|----------------|
| Radiotherapy    | -0.483  | 0.201    | 5.803      | 0.016   | 0.617 | 0.416 - 0.914  |
| Chemotherapy    | -0.672  | 0.161    | 17.414     | < 0.001 | 0.511 | 0.373 - 0.700  |
| LNR             | 0.398   | 0.169    | 5.512      | 0.019   | 1.488 | 1.068 - 2.074  |
| Tumor size      | 0.453   | 0.157    | 8.299      | 0.004   | 1.573 | 1.156 - 2.140  |

ASCP, adenosquamous carcinoma of the pancreas; HR, hazard ratio; CI, confidence interval; LNR, Lymph node ratio.
FIGURE 1

(A) The nomogram for predicting the overall survival of patients with pancreatic adenosquamous carcinoma. (B–E) The 1-year and 2-year calibration curves of the development group and the internal verification group for prognostic nomogram of patients with pancreatic adenosquamous carcinoma (B) 1-year development group (C) 2-year development group (D) 1-year internal verification group (E) 2-year internal verification group.
FIGURE 2
(A–D) The 1-year and 2-year receiver-operating characteristic (ROC) curve of the development group and the internal verification group for the nomogram and AJCC TNM (8th) staging system of patients with pancreatic adenosquamous carcinoma. (A) 1-year development group (B) 2-year development group (C) 1-year internal verification group (D) 2-year internal verification group. (E, F) The 1-year and 2-year overall survival Decision Curve Analysis (DCA) of the nomogram and AJCC TNM (8th) staging system of patients with pancreatic adenosquamous carcinoma. (E) 1-year overall survival (F) 2-year overall survival. AJCC, American Joint Committee on Cancer.

FIGURE 3
(A–C): Kaplan-Meier analysis between different nomogram total scores predicting patients with pancreatic adenosquamous carcinoma in the (A): development cohort, (B): internal validation cohort, (C): external validation cohort.
patient’s tumor. Tumor microenvironment and molecular features of ASCP could be our next research topic. Considering this, the nomogram prediction model established in this study can be used for future research.

Conclusion

Here we developed a nomogram especially for ASCP to predict the survival and prognosis. Univariate and multivariate analysis showed that four parameters, including tumor size, radiotherapy, chemotherapy, and LNR, could influence the survival of ASCP patients. In addition, by comparing the nomogram’s efficiency with AJCC TNM (8th) staging system, it was proved that the nomogram is superior to the TNM stage in predicting the prognosis. Finally, we applied the external cohort from multi-center to verify the performance and get satisfactory results. Our nomogram has clinical applicability.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by The Institutional Review Boards of the First Affiliated Hospital of Xi’an Jiaotong University. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

Conception and design: ZWa, YS, ZWu, and QM. Administrative support: ZWang, ZWu, YM, XY, and LH. Provision of study materials or patients: CR, ZWang, JJ, and YS. Collection and assembly of data: CR, YM, JJ, JD, YJ, YW, and ZWang. Data analysis and interpretation: CR, YM, ZWang, WL, YS, JD, YJ, and YW. Manuscript writing: all authors. Final approval of manuscript: all authors.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2022.927107/full#supplementary-material

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