Asia-Pacific Journal of Oncology Nursing 9 (2022) 100141

Contents lists available at ScienceDirect

Asia-Pacific Journal of Oncology Nursing

journal homepage: www.apjon.org

Original Article

Machine learning models for predicting survival in patients with ampullary adenocarcinoma

Tao Huang [a,1], Liying Huang [a,1], Rui Yang [a], Shuna Li [a], Ningxia He [a], Aozi Feng [a], Li Li [a], Jun Lyu [a,b,*]

[a] Department of Clinical Research, The First Affiliated Hospital of Jinan University, Guangzhou, China
[b] Guangdong Provincial Key Laboratory of Traditional Chinese Medicine Informatization, Guangzhou, China

ARTICLE INFO

Keywords:
Ampullary adenocarcinoma
Survival analysis
Machine learning
Risk factor
SEER

ABSTRACT

Objective: The aim of this study was to predict the long-term survival probability of patients with ampullary adenocarcinoma (AAC), which would provide a theoretical basis for the long-term care of these patients.
Methods: Data on patients with AAC during 2004–2015 were obtained from the Surveillance, Epidemiology, and End Results database, which were split at a 7:3 ratio into two independent cohorts: training and testing cohorts. Differences in survival between the two groups were tested using the Kaplan–Meier estimator and log-rank test methods. We constructed six survival analysis methods: the American Joint Committee on Cancer TNM stage, Cox Proportional Hazards regression, CoxTime, DeepSurv, XGBoost Survival Embeddings, and Random Survival Forest. The performances of these models were evaluated using the C-index, receiver operating characteristic (ROC), and calibration curves.
Results: This study included 2,935 patients with AAC. Univariate Cox regression analyses of the training cohort indicated that race, marital status at diagnosis, scope of regional lymph node surgery, tumor grade, summary stage, American Joint Committee on Cancer stage, TNM stage T, and TNM stage N were important factors affecting survival ($P < 0.05$). The results of the C-index indicated that DeepSurv performed the best among the six models, with the highest C-index of 0.731. The areas under the ROC curves of the DeepSurv model at the 1-year, 3-year, 5-year, and 10-year time points were 0.823, 0.786, 0.803, and 0.813, respectively. The calibration curve indicated that DeepSurv performed well, with good calibration.
Conclusions: Machine learning models such as DeepSurv have a stronger performance in the survival analysis of patients with AAC.

Introduction

Ampullary adenocarcinoma (AAC), which constitutes approximately 0.2% of gastrointestinal cancers, is an uncommon but aggressive type of periampullary cancer that originates in biliary, duodenal, or pancreatic ductal epithelial cells.[1,2] The incidence of AAC is estimated to be 0.5, 0.73, and 0.96 per 100,000 persons per year in the US, Japan, and the Netherlands, respectively.[3–5] Despite its rarity, the occurrence of AAC has increased worldwide over the past few decades.[6,7] Patients with AAC tend to present typical symptoms of biliary obstruction at relatively early stages, but these symptoms are mostly non-specific and are therefore often detected incidentally during examinations.[8,9] Although the early detection of symptoms helps to improve the resection rates in radical surgery, which is the standard treatment for AAC, high risks of recurrence, and postoperative mortality are major concerns.[10,11] Different centers have reported a wide range of 5-year overall survival (OS) rates after AAC resection of 32%–69.1%, with a median survival time of 28–70 months, while the 10-year OS rate ranged from 26% to 48%.[4,12,13] High-quality evidence from clinical trials of AAC is currently inadequate, and relevant data are mostly collected from subgroup analyses of pancreaticobiliary malignancies or retrospective analyses.[14] Specific treatment decisions and prognoses of AAC are under discussion including the construction of the American Joint Committee on Cancer (AJCC) TNM staging system.[10] Knowledge of the prognostic factors associated with different survival outcomes among patients with AAC is important for survival predictions and nursing planning.[4,15,16]

* Corresponding author.
E-mail address: lyujun2020@jnu.edu.cn (J. Lyu).
[1] These authors have contributed equally to this work as joint first author.

https://doi.org/10.1016/j.apjon.2022.100141
Received 29 July 2022; Accepted 30 August 2022

Previous research has used various types of prediction models to assess the short-term survival rates of AAC, including Kaplan–Meier survival analysis, logistic regression, and the Cox proportional hazards (CoxPH) model.[5–13,16–23] Kaplan–Meier survival analysis is the most commonly method used to investigate the prognostic factors for AAC, which does not allow adjustments for confounders and has a restrictive assumption of non-informative censoring.[24,25] Logistic regression models aim to estimate the relationship between potential factors and survival outcomes as well as adjust for confounders.[26,27] However, this method does not consider survival time, which might affect prediction accuracy.[28] The CoxPH model is commonly used to explore the effects of joint covariates on OS, but it is based on hazard ratios (HRs) being constant over time and linear effects of covariates on hazards, which might not be applicable to real-life applications.[29] It is therefore necessary to develop a new and more accurate model for predicting the survival rate in AAC.

With the rapid development of computer technology and increasing focus on personalized treatment, machine learning[30] techniques can process large volumes of patient medical records or data without overly restrictive conditions, which can improve the accuracy and reliability of survival predictions.[31] Deep learning is a new machine learning technique that utilizes artificial neural networks to extract patterns and make predictions from high-dimension data.[32] It shows a great potential in the healthcare field, with good performance in the early detection of cancer.[33] Although machine learning techniques are widely used for survival predictions in various cancers, few studies have applied them to determining the diagnosis, prognosis, or treatment in AAC. In this study, a traditional survival analysis method was constructed and compared with several common machine learning models. An optimal model for predicting the survival outcome of patients with AAC was established, which might help specific treatment decisions and personalized nursing planning for AAC.

Methods

Data source

Data from 2004 to 2015 were collected from the Surveillance, Epidemiology, and End Results (SEER)[34,35] 17 database using the SEER*Stat software (version 8.4.0.1), which was submitted in November 2021 and published in April 2022.[34] The SEER 17 database collects and publishes cancer incidence and survival data from population-based cancer registries that cover approximately 26.5% of the US population. This study collected information of patients diagnosed with AAC after receiving permission to access the SEER 17 database through a multiple-step request process.

Study population and inclusion criteria

The study investigated patients diagnosed with AAC during 2004–2015 as defined by the International Classification of Diseases for Oncology, third edition. Patients with AAC were identified using a primary site code (ampulla of vater [C24.1]) and morphology code (adenocarcinoma, NOS [8140/3]). Among these patients, the exclusion criteria included having no data on tumor grade, diagnostic confirmation, AJCC TNM stage, surgery information, or marital status at diagnosis. The information of 2,935 patients with AAC were collected, including age, sex, race, marital status at diagnosis, scope of regional lymph node surgery, tumor grade, summary stage, AJCC TNM stage, surgery status, radiotherapy, chemotherapy, tumor extent, regional lymph node involvement and metastasis, primary indicator of first malignancy, vital status, and survival time. These patients were subsequently randomly divided into the training and testing cohorts with a ratio of 7:3. Steps in this study to select AAC cases under these criteria and screening procedure are illustrated in Fig. 1.

Survival analysis models

The AJCC TNM staging system is a conventional diagnostic model that was used as the baseline model in this study. We performed univariate analyses of patient indicators using the traditional CoxPH regression model,[36] screened out meaningful indicators ($P < 0.05$), and then used multivariate analysis to determine the ability of survival predictive of the Cox model. The four other survival analysis models used in this study included two learning models based on decision tree ensembles [XGBoost Survival Embeddings (XGBSE)[37] and random survival forest (RSF)[38]] and two deep learning models based on neural network structures (CoxTime[39] and DeepSurv[40]). All of the models were simulated using Python (version 3.9) software, and the Bayesian optimizer[41] (Bayesian-optimization version 1.2.0) was used to optimize the model parameters. Among them, XGBSE and RSF used the XGBSE (version 0.2.3) and random survival forest (version 0.8.0) packages, respectively, and both CoxTime and DeepSurv were implemented using pycox (version 0.2.3).

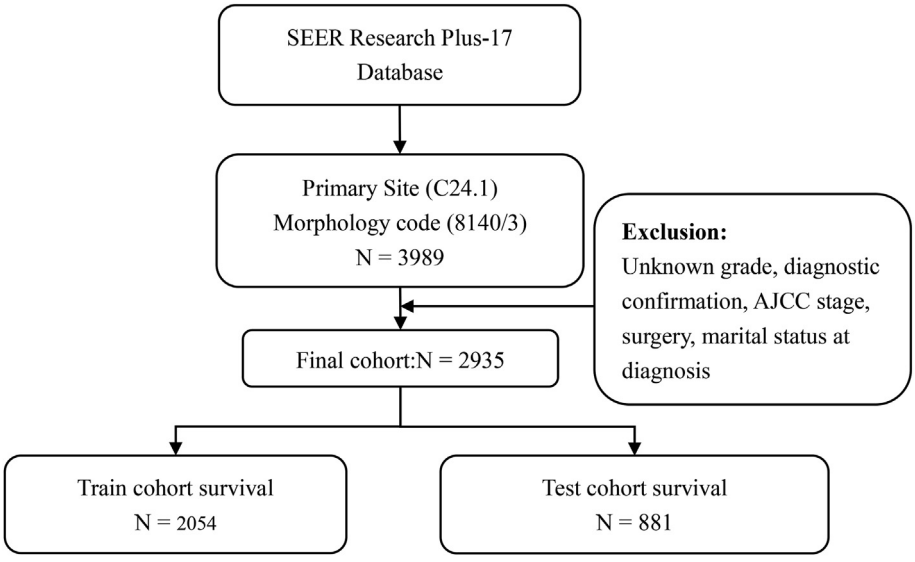


Fig. 1. Flow diagram of patients with ampullary adenocarcinoma selection. AJCC, American Joint Committee on Cancer; SEER, Surveillance, Epidemiology, and End Results.

Table 1
Analysis of the main characteristics of patients with ampullary adenocarcinoma.

Variables	Overall	Train cohort	Test cohort	*P*-value
	N (%)	*N* (%)	*N* (%)	
Patients	2935 (100.0%)	2054 (70.0%)	881 (30.0%)	
Age (years)				0.593
Median (IQR)	69.0 [59.0, 77.0]	69.0 [59.0, 77.0]	69.0 [59.0, 77.0]	
Gender				0.551
Male	1,683 (57.3%)	1,170 (57.0%)	513 (58.2%)	
Female	1,252 (42.7%)	884 (43.0%)	368 (41.8%)	
Race				0.618
White	2,322 (79.1%)	1,632 (79.5%)	690 (78.3%)	
Black	211 (7.2%)	149 (7.3%)	62 (7.0%)	
Others	402 (13.7%)	273 (13.3%)	129 (14.6%)	
Marital status at diagnosis				0.138
Married	1,841 (62.7%)	1,269 (61.8%)	572 (64.9%)	
Single	381 (13.0%)	265 (12.9%)	116 (13.2%)	
DSW	713 (24.3%)	520 (25.3%)	193 (21.9%)	
Scope of regional lymph node surgery				0.771
None	688 (23.4%)	491 (23.9%)	197 (22.4%)	
1 to 3	172 (5.9%)	121 (5.9%)	51 (5.8%)	
4 or more	2,037 (69.4%)	1,417 (69.0%)	620 (70.4%)	
Unknown or not applicable	38 (1.3%)	25 (1.2%)	13 (1.5%)	
Grade				0.882
Grade I	332 (11.3%)	228 (11.1%)	104 (11.8%)	
Grade II	1,579 (53.8%)	1,101 (53.6%)	478 (54.3%)	
Grade III	999 (34.0%)	707 (34.4%)	292 (33.1%)	
Grade IV	25 (0.9%)	18 (0.9%)	7 (0.8%)	
Summary stage				0.207
Localized	394 (13.4%)	290 (14.1%)	104 (11.8%)	
Regional	1,944 (66.2%)	1,355 (66.0%)	589 (66.9%)	
Distant	597 (20.3%)	409 (19.9%)	188 (21.3%)	
AJCC				0.765
I	828 (28.2%)	589 (28.7%)	239 (27.1%)	
II	1,066 (36.3%)	748 (36.4%)	318 (36.1%)	
III	720 (24.5%)	496 (24.1%)	224 (25.4%)	
IV	321 (10.9%)	221 (10.8%)	100 (11.4%)	
T				0.110
T1	522 (17.8%)	386 (18.8%)	136 (15.4%)	
T2	749 (25.5%)	504 (24.5%)	245 (27.8%)	
T3	799 (27.2%)	564 (27.5%)	235 (26.7%)	
T4	810 (27.6%)	559 (27.2%)	251 (28.5%)	
TX	55 (1.9%)	41 (2.0%)	14 (1.6%)	
N				0.863
N0	1,541 (52.5%)	1,076 (52.4%)	465 (52.8%)	
N1	1,331 (45.3%)	932 (45.4%)	399 (45.3%)	
NX	63 (2.1%)	46 (2.2%)	17 (1.9%)	
M				0.685
M0	2,614 (89.1%)	1,833 (89.2%)	781 (88.6%)	
M1	321 (10.9%)	221 (10.8%)	100 (11.4%)	
Surgery performed				0.560
Yes	2,314 (78.8%)	1,613 (78.5%)	701 (79.6%)	
No	621 (21.2%)	441 (21.5%)	180 (20.4%)	
Radiotherapy				0.615
Yes	621 (21.2%)	429 (20.9%)	192 (21.8%)	
No/Unknown	2,314 (78.8%)	1,625 (79.1%)	689 (78.2%)	
Chemotherapy				0.954
Yes	1,270 (43.3%)	890 (43.3%)	380 (43.1%)	
No/Unknown	1,665 (56.7%)	1,164 (56.7%)	501 (56.9%)	
CS extension				0.118
Localized	522 (17.8%)	386 (18.8%)	136 (15.4%)	
Regional	2,062 (70.3%)	1,427 (69.5%)	635 (72.1%)	
Distant	296 (10.1%)	200 (9.7%)	96 (10.9%)	
Unknown	55 (1.9%)	41 (2.0%)	14 (1.6%)	
CS lymph nodes involvement				0.863
Yes	1,331 (45.3%)	932 (45.4%)	399 (45.3%)	
No/Unknown	1,604 (54.7%)	1,122 (54.6%)	482 (54.7%)	
CS Mets at DX				0.685
Yes	321 (10.9%)	221 (10.8%)	100 (11.4%)	
No	2,614 (89.1%)	1,833 (89.2%)	781 (88.6%)	
First malignant primary indicator				0.361
Yes	2,425 (82.6%)	1,688 (82.2%)	737 (83.7%)	
No	510 (17.4%)	366 (17.8%)	144 (16.3%)	
Status				0.453
Alive	764 (26.0%)	526 (25.6%)	238 (27.0%)	
Death	2,171 (74.0%)	1,528 (74.4%)	643 (73.0%)	

AJCC, American Joint Committee on Cancer.

Data analysis

Statistical analysis of patient data in this study was performed using Python software.[42] The Kruskal–Wallis rank-sum or Mann–Whitney U tests were used to assess the distributions of the variables. Continuous variables that were not normally distributed were expressed as medians and 25th–75th percentiles, and categorical variables were expressed as percentages of the population. The Kaplan–Meier method was used to draw survival curves, and group survival differences were compared using the log-rank test. The C-index and area under the receiver operating characteristic (ROC) curve (AUC) were used to evaluate the predictive abilities of the models. Calibration plots were used to assess the relationship between follow-up outcomes and predicted survival probability.

Results

Baseline characteristics of the patients

The sample population comprised 2,935 patients with AAC, of which 1,683 (57.3% of the sample population) patients were male and 1,252 (42.7%) were female. The mean age was 69 years, males accounted for about 14% more of the population than did females (57.0% vs 43.0%), and 1,632 (79.5%) patients were white. Patients were followed for a maximum of 190 months, with a mean of 42 months. The overall patient follow-up mortality rate was 74.0%.

Table 1 lists the basic characteristics and variance analysis results for the total study population as well as in the training and testing cohorts. The training cohort consisted of 2,054 patients (70%). The log-rank test used to assess the difference between the two cohorts yielded $P = 0.736$, and the survival curves did not differ significantly between the two cohorts. Kaplan–Meier analysis curves of the training and testing cohorts are shown in Fig. 2.

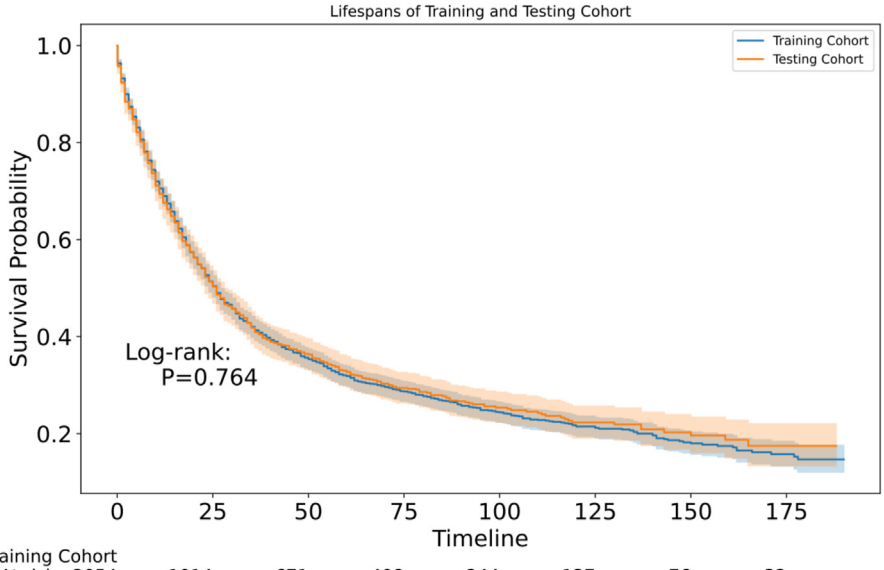
Risk factors identified by Cox model

All variables in Table 1 were subjected to univariate Cox analyses, which revealed that race, marital status at diagnosis, scope of regional lymph node surgery, tumor grade, summary stage, AJCC stage, TNM stage T, and TNM stage N were risk factors for patients with AAC. These factors were subsequently included in a multivariate Cox analysis. Table 2 lists the results of univariate and multivariate analyses. Combined with Table 1, it can be seen that the mortality risk of patients with AAC was not related to age or sex, but was related to race. Compared with white patients, black patients had a higher mortality risk (HR = 1.25, 95% confidence interval [CI] = 1.01–1.55, $P = 0.042$), while other races had lower mortality risks than whites (HR = 0.73, 95% CI = 0.61–0.87, $P = 0.001$). Patients with Divorced/Separated/Widowed had a higher mortality risk than patients who were married (HR = 1.24, 95% CI = 1.08–1.41, $P = 0.002$). Regardless of its degree, lymph node surgery reduced the mortality risk relative to no surgery ($P > 0.05$). The cancer status of the patient, including tumor grade, summary stage, and AJCC TNM stage, were consistent with the basic understanding. The risk of mortality increased with the tumor grade and stage.

Model comparison of survival analysis

We used the training cohort to construct six survival analysis models and adjust the parameters to their best states. Model performance was then evaluated using a testing cohort that was completely isolated from the training cohort. Harrell's C-index was first used to measure the relationship between model-predicted risk profiles and actual patient survival, reflecting the predictive power of the models. The AJCC TNM stage model had the worst result in predicting the survival of patients with AAC, with a C-index of only 0.606, followed by the CoxPH model (0.693) and then XGBSE (0.709) and RSF (0.716). The C-indexes of the deep learning model based on the neural network were 0.714 for CoxTime and 0.731 for DeepSurv.

We calculated the 1-year, 3-year, 5-year, and 10-year ROC curves of all models to verify the recognition ability of the models. Fig. 3 shows the ROC assessments of the survival analysis model at different time points, representing the overall performance of the model. The AJCC TNM stage model had the worst performance in predicting patient survival, with AUCs of only 0.622, 0.664, 0.674, and 0.655 at 1 year, 3 years, 5 years, and 10 years, respectively, but the ROC curve of the DeepSurv model



Training Cohort								
At risk	2054	1014	671	408	244	137	76	32
Censored	0	30	73	223	335	415	459	496
Events	0	1010	1310	1423	1475	1502	1519	1526
Testing Cohort								
At risk	881	430	296	188	98	60	29	7
Censored	0	17	32	89	157	185	211	231
Events	0	434	553	604	626	636	641	643

Fig. 2. Kaplan–Meier curve of train and test cohorts. There was no statistically significant difference between the survival of train and test cohorts in the log-rank test ($P = 0.764$).

Table 2
Survival predictors in Cox PH model.

Analysis variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Race						
White	Reference			Reference		
Black	1.22	0.98–1.51	0.069	1.25	1.01–1.55	0.042
Others	0.72	0.60–0.86	< 0.001	0.73	0.61–0.87	0.001
Marital status at diagnosis						
Married	Reference			Reference		
Single	1.07	0.90–1.28	0.459	1.06	0.89–1.27	0.506
DSW	1.41	1.24–1.60	< 0.001	1.24	1.08–1.41	0.002
Scope of regional lymph node surgery						
None	Reference			Reference		
1 to 3	0.43	0.34–0.55	< 0.001	0.39	0.30–0.51	< 0.001
4 or more	0.26	0.23–0.30	< 0.001	0.21	0.18–0.25	< 0.001
Unknown or not applicable	0.27	0.16–0.46	< 0.001	0.21	0.12–0.36	< 0.001
Grade						
Grade I	Reference			Reference		
Grade II	1.16	0.96–1.4	0.126	1.13	0.93–1.37	0.231
Grade III	1.64	1.35–2.00	< 0.001	1.54	1.26–1.88	< 0.001
Grade IV	1.03	0.54–1.96	0.924	1.04	0.55–2.00	0.897
Summary stage						
Localized	Reference			Reference		
Regional	1.01	0.85–1.20	0.897	1.01	0.68–1.49	0.974
Distant	2.14	1.76–2.60	< 0.001	1.01	0.64–1.59	0.982
AJCC						
I	Reference			Reference		
II	1.29	1.11–1.49	0.001	1.39	1.04–1.87	0.025
III	1.90	1.62–2.23	< 0.001	1.84	1.15–2.94	0.011
IV	4.60	3.79–5.59	< 0.001	1.76	1.15–2.71	0.010
T						
T1	Reference			Reference		
T2	0.67	0.56–0.81	< 0.001	0.94	0.69–1.30	0.726
T3	1.06	0.90–1.26	0.491	1.18	0.89–1.56	0.247
T4	1.43	1.21–1.68	< 0.001	1.12	0.76–1.65	0.569
TX	3.81	2.58–5.63	< 0.001	1.08	0.67–1.73	0.758
N						
N0	Reference			Reference		
N1	1.25	1.12–1.41	< 0.001	1.31	1.13–1.53	0.001
NX	4.21	2.99–5.94	< 0.001	1.25	0.85–1.83	0.254

AJCC, American Joint Committee on Cancer.

partially intersected with those of the CoxTime and RSF models. However, the DeepSurv model had the largest total AUC, and the predicted AUCs for 1-year, 3-year, 5-year, and 10-year survival probabilities were 0.823, 0.786, 0.803, and 0.813, respectively. This indicates that the DeepSurv model has better classification and discriminative abilities; the model was more accurate in predicting the survival prognoses of patients with AAC.

Fig. 4 compares the results of the six models in predicting patient survival with actual survival at 1 year, 3 years, 5 years, and 10 years. The closer to the standard 45-degree diagonal, the better the prediction. The results indicated that the AJCC and CoxPH models were significantly different. RSF and XGBSE fitted the 45-degree diagonal best, followed by DeepSurv and CoxTime.

Discussion

AAC is gastrointestinal cancer with a high mortality rate.[4,12,13] Although rare, its incidence has increased in recent decades.[6,7] High recurrence and postoperative mortality risks are major prognostic issues in patients with AAC.[10,11] Various genotypes and tumor stages that affect the prognosis of patients with AAC have recently been found.[4,15,16] However, the available prediction models have both advantages and disadvantages. The CoxPH model is currently the most widely used predictive model in the field of survival analysis.[43,44] This model requires each predictor to be a linear factor and for the effect of covariates on survival to not change over time. It ignores the impact of some non-linear factors on patient survival outcomes. However, tumor development and its changes are affected by many different factors, and traditional strictly linear models are unlikely to accurately predict the prognoses of patients with cancer. It is therefore necessary to develop new methods to incorporate both linear and non-linear factors, and so in this study, we constructed and validated a deep learning model for predicting the mortality risk of patients with AAC by comparing multiple different types of survival analysis models.

According to the analysis results of the CoxPH regression model, race, marital status at diagnosis, scope of regional lymph node surgery, tumor grade, summary stage, and AJCC TNM stage are the main factors affecting patient survival. Racial disparities in patients with cancer have always been one of the focuses of research.[45–48] Among patients with AAC in the US population of this study, black patients had a higher mortality risk. Because cancer treatment is expensive, this finding might be related to the medical insurance or financial status of the patient,[49,50] and patients with AAC with worse statuses receive worse care.[51] Marital status has also been found to be a risk factor for various diseases,[52] and single patients (including those who are single, divorced, separated, or widowed) have a higher mortality risk than those in a relationship, which may be related to the lack of care that the patient received.[53] The present study found that surgical resection of metastatic lymph nodes is beneficial to patient outcomes, which is consistent with previous studies.[13,54] The grade and stage of cancer determine the severity of the patient, and more patients with more-severe conditions have a worse prognosis and may require more careful care.

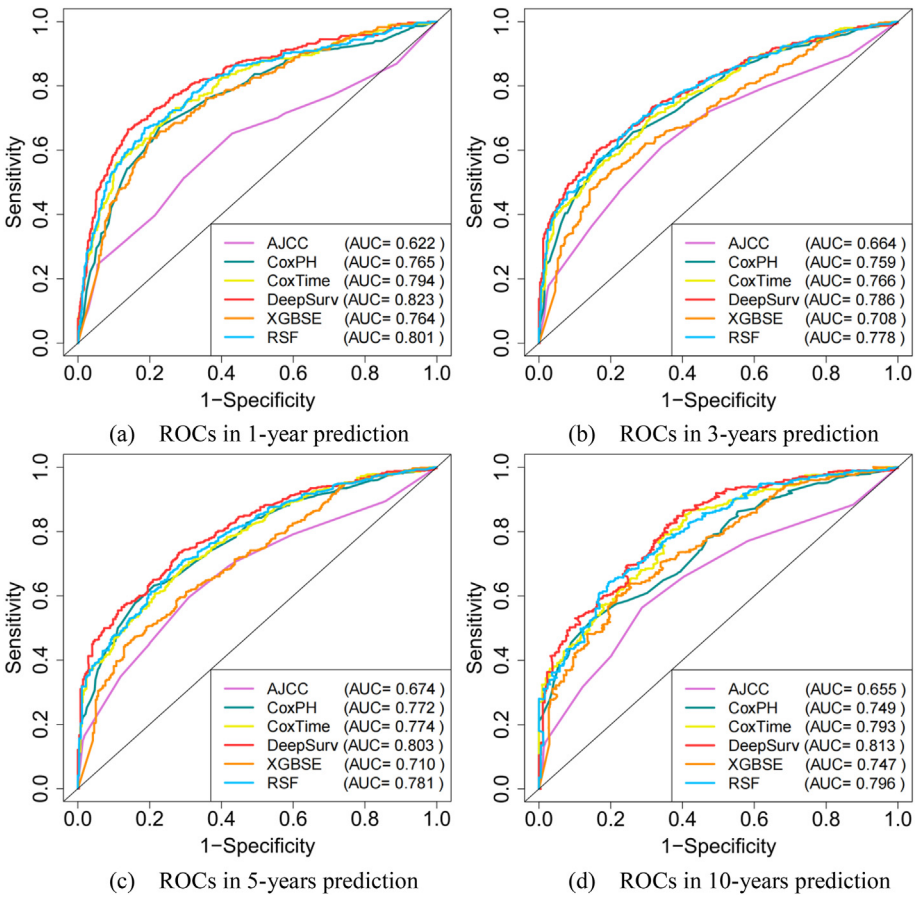


Fig. 3. ROC plot. Comparison of ROC in six models at (**a**) 1-year, (**b**) 3-years, (**c**) 5-years, and (**d**) 10-years in testing cohort population. AJCC, American Joint Committee on Cancer; ROC: receiver operating characteristic; AUC: area under curve.

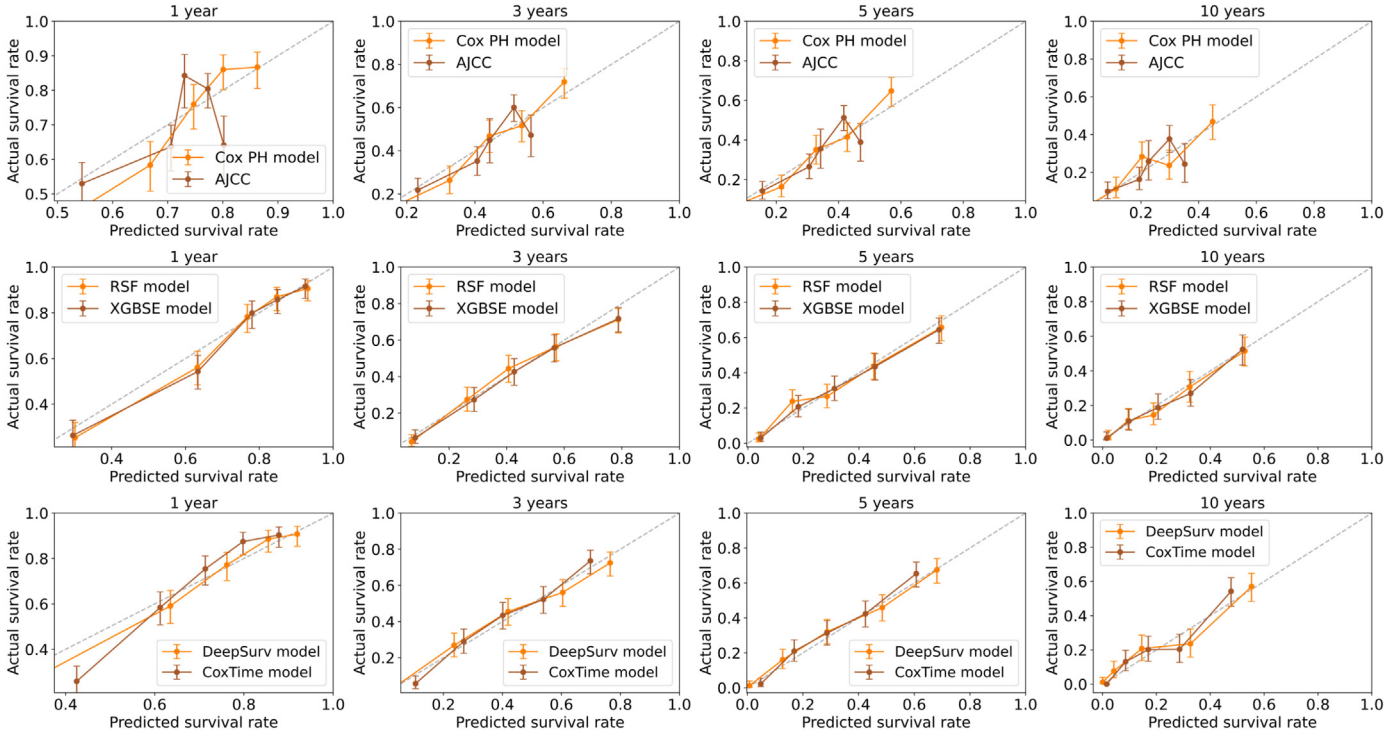


Fig. 4. Calibration plot. AJCC, American Joint Committee on Cancer.

The CoxPH model identified the main factors affecting patient outcomes. Adding these factors as covariates resulted in the model performing better than models using only AJCC TNM staging. However, due to too many constraints, the predictive ability cannot be further improved. In contrast, the decision-tree-based ensemble machine learning models (XGBSE and RSF) can automatically deal with a series of problems caused by the restrictive assumption of CoxPH and had achieved better evaluation results and a stronger ability to predict the survival of patients with AAC (with a higher C-index). The deep learning models (CoxTime and DeepSurv) also obtained the best prediction results due to the powerful non-linear fitting ability of their multilayer neuron-like structures. Comparing ROC curves at different time points revealed that these models also performed well, which was consistent with the performance of DeepSurv in predicting other diseases. The calibration of DeepSurv was no better than that of RSF or XGBSE. Compared with previous research,[55] it was assumed that this was due to there being insufficient data. Deep learning involves data-driven models, and a larger amount of data results in better model performance.[56] At the same time, we believe that less data are available than in this study, the RSF model may be a better choice. In this study, the calibration curve of DeepSurv was acceptable. DeepSurv had a good predictive ability for the survival outcomes of patients with AAC.

This study had certain limitations. First, the SEER database does not contain detailed information about the views of a patient related to treatment types, such as whether the tumor was surgically removed, the type of chemotherapy, religious beliefs, and education. This undisclosed information may affect the prognosis of a patient. Second, the developed model needs to be verified externally in different centers. Validating the model in different regions and hospital centers can increase the robustness of the model. Finally, deep learning survival analysis models are difficult to interpret since it is difficult to accurately understand the internal computing process of these models. Future research should strive to address these issues.

Conclusions

In this study, CoxPH regression analysis was used to determine the risk factors affecting the prognosis of patients with AAC. These factors included race, marital status at diagnosis, scope of regional lymph node surgery, tumor grade, summary stage, AJCC stage, TNM stage T, and TNM stage N. We compared six survival prediction models and found that DeepSurv is most accurate at predicting the prognoses and survival times of patients with AAC.

Author contributions

Conceived and designed the analysis: Tao Huang, Liying Huang, Rui Yang.

Collected the data: Liying Huang.

Experimental results and manuscripts review and medical guidance: Rui Yang.

Statistical theory guidance: Shuna Li, Ningxia He.

Validation: Aozi Feng, Li Li.

Supervision, project administration: Jun Lyu.

Wrote the paper: Tao Huang, Liying Huang.

Declaration of competing interest

None declared.

Funding

The study was supported by Guangdong Provincial Key Laboratory of Traditional Chinese Medicine Informatization (Grant No. 2021B1212040007).

Ethics statement

The data of this study comes from the SEER database. The SEER database is a tumor-related database developed by the National Cancer Institute of the United States, providing research data for researchers free of charge. All patients participating in the study received the ethical approval sought by the National Cancer Institute. The informed consent was obtained from all patients or, if patients are under 18, from a parent and/or legal guardian. The use of all data in the study follows the National Cancer Institute's data use statement. The research content follows the statement of the National Cancer Institute guidelines.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apjon.2022.100141.

References

1. Tsai YE, Chien KH, Li YF, Lai SW. Rare orbital metastasis originating from ampullary adenocarcinoma. *Medicina (Kaunas)*. 2021;57(11).
2. Cheng J, Mao Y, Hong W, et al. Multimodal data analysis reveals that pancreatobiliary-type ampullary adenocarcinoma resembles pancreatic adenocarcinoma and differs from cholangiocarcinoma. *J Transl Med*. 2022;20(1):272.
3. May M, Raufi AG, Sadeghi S, et al. Prolonged response to HER2-directed therapy in three patients with HER2-amplified metastatic carcinoma of the biliary system: case study and review of the literature. *Oncol*. 2021;26(8):640–646.
4. Okano K, Oshima M, Suto H, et al. Ampullary carcinoma of the duodenum: current clinical issues and genomic overview. *Surg Today*. 2022;52(2):189–197.
5. de Jong EJM, van der Geest LG, Besselink MG, et al. Treatment and overall survival of four types of non-metastatic periampullary cancer: nationwide population-based cohort study. *HPB*. 2022. Oxford.
6. Utsumi M, Kitada K, Tokunaga N, et al. A combined prediction model for biliary tract cancer using the prognostic nutritional index and pathological findings: a single-center retrospective study. *BMC Gastroenterol*. 2021;21(1):375.
7. Sweed D, Taha M, Abd Elhamed S, El Dein Mohamed AS. The prognostic role of CD73/A2AR expression and tumor immune response in periampullary carcinoma subtypes. *Asian Pac J Cancer Prev APJCP*. 2022;23(4):1239–1246.
8. Zhang X, Sun C, Li Z, et al. Development and validation of a new lymph node ratio-based staging system for ampullary carcinoma after curative pancreaticoduodenectomy. *Front Oncol*. 2021;11, 811595.
9. Watanabe A, Harimoto N, Araki K, et al. FDG-PET for preoperative evaluation of tumor invasion in ampullary cancer: a retrospective analysis. *J Surg Oncol*. 2021;124(3):317–323.
10. Wang SJ, Li YF, Liao S, Wei YZ, Zhou YM. Proposal of a new T-stage classification system for ampullary carcinoma based on Surveillance, Epidemiology and End Result (SEER) database. *Hepatobiliary Pancreat Dis Int*. 2021;20(6):568–573.
11. Hwang JS, So H, Oh D, et al. Long-term outcomes of endoscopic patellectomy for early-stage cancer in duodenal ampullary adenoma: comparison to surgical treatment. *J Gastroenterol Hepatol*. 2021;36(8):2315–2323.
12. Park YM, Seo HI. Predictive value of metabolic activity detected by pre-operative 18F FDG PET/CT in ampullary adenocarcinoma. *Medicine (Baltim)*. 2021;100(42), e27561.
13. Vilhordo DW, Gregório C, Valentini Jr DF, Edelweiss MIA, Uchoa DM, Osvaldt AB. Prognostic factors of long-term survival following radical resection for ampullary carcinoma. *J Gastrointest Cancer*. 2021;52(3):872–881.
14. Taliente F, Bianco G, Moschetta G, et al. From endoscopic resection to pancreatoduodenectomy: a narrative review of treatment modalities for the tumors of the ampulla of Vater. *Chin Clin Oncol*. 2022;11(3):23.
15. Patel M, Uboha NV. Treatment approach to adenocarcinoma of the ampulla of vater. *Curr Treat Options Oncol*. 2021;22(11):103.
16. Fernandez-Placencia RM, Montenegro P, Guerrero M, et al. Survival after curative pancreaticoduodenectomy for ampullary adenocarcinoma in a South American population: a retrospective cohort study. *World J Gastrointest Surg*. 2022;14(1):24–35.
17. Chakraborty S, Ecker BL, Seier K, et al. Genome-derived classification signature for ampullary adenocarcinoma to improve clinical cancer care. *Clin Cancer Res*. 2021;27(21):5891–5899.
18. Sekine M, Watanabe F, Ishii T, et al. Investigation of the indications for endoscopic papillectomy and transduodenal ampullectomy for ampullary tumors. *J Clin Med*. 2021;10(19).
19. Nappo G, Galvanin J, Gentile D, et al. Long-term outcomes after pancreatoduodenectomy for ampullary cancer: the influence of the histological subtypes and comparison with the other periampullary neoplasms. *Pancreatology*. 2021;21(5):950–956.
20. Shyr YM, Wang SE, Chen SC, Shyr BU, Shyr BS. Robotic pancreaticoduodenectomy for pancreatic head cancer and periampullary lesions. *Ann Gastroenterol Surg*. 2021;5(5):589–596.
21. So H, Ko SW, Shin SH, Kim EH, Park DH. Impact of 5-year endoscopic surveillance intervals with biopsy following endoscopic papillectomy for ampullary adenoma. *J Personalized Med*. 2022;12(1).

22. van Roessel S, Soer EC, Daamen LA, et al. Preoperative misdiagnosis of pancreatic and periampullary cancer in patients undergoing pancreatoduodenectomy: a multicentre retrospective cohort study. *Eur J Surg Oncol*. 2021;47(10):2525–2532.
23. Meunier C, Lisotti A, Gupta V, et al. Oral anticoagulants but not antiplatelet agents increase the risk of delayed bleeding after endoscopic patellectomy: a large study in a tertiary referral center. *Surg Endosc*. 2022.
24. D'Arrigo G, Leonardis D, Abd ElHafeez S, Fusaro M, Tripepi G, Roumeliotis S. Methods to analyse time-to-event data: the Kaplan-Meier survival curve. *Oxid Med Cell Longev*. 2021;2021, 2290120.
25. Fojo T, Simon RM. Inappropriate censoring in Kaplan-Meier analyses. *Lancet Oncol*. 2021;22(10):1358–1360.
26. Zabor EC, Reddy CA, Tendulkar RD, Patil S. Logistic regression in clinical studies. *Int J Radiat Oncol Biol Phys*. 2022;112(2):271–277.
27. Schober P, Vetter TR. Logistic regression in medical research. *Anesth Analg*. 2021; 132(2):365–366.
28. Churpek MM, Yuen TC, Winslow C, Meltzer DO, Kattan MW, Edelson DP. Multicenter comparison of machine learning methods and conventional regression for predicting clinical deterioration on the wards. *Crit Care Med*. 2016;44(2):368–374.
29. Pang M, Platt RW, Schuster T, Abrahamowicz M. Flexible extension of the accelerated failure time model to account for nonlinear and time-dependent effects of covariates on the hazard. *Stat Methods Med Res*. 2021;30(11):2526–2542.
30. Wang P, Li Y, Reddy CK. Machine learning for survival analysis: a survey. *ACM Comput Surv*. 2019;51(6):110.
31. Egger J, Gsaxner C, Pepe A, et al. Medical deep learning-A systematic meta-review. *Comput Methods Progr Biomed*. 2022;221, 106874.
32. Tran KA, Kondrashova O, Bradley A, Williams ED, Pearson JV, Waddell N. Deep learning in cancer diagnosis, prognosis and treatment selection. *Genome Med*. 2021; 13(1):152.
33. Triantafyllidis A, Kondylakis H, Katehakis D, et al. Deep learning in mHealth for cardiovascular disease, diabetes, and cancer: systematic review. *JMIR Mhealth Uhealth*. 2022;10(4), e32344.
34. Institute NC. Surveillance, epidemiology, and end results program (SEER). *Cancer Statistics Statistical Summaries*. 2017.
35. Yang J, Li Y, Liu Q, et al. Brief introduction of medical database and data mining technology in big data era. *J Evid Base Med*. 2020;13(1):57–69.
36. Fox J, Weisberg S. Cox proportional-hazards regression for survival data. *An R and S-PLUS companion to applied regression*. 2002;2002.
37. Vieira D, Gimenez G, Marmorela G, Estima V. XGBoost survival Embeddings: improving statistical properties of XGBoost survival analysis implementation. *Loft Python*. 2021.
38. Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. *Ann Appl Stat*. 2008;2(3):841–860.
39. Kvamme H, Ø Borgan, Scheel I. Time-to-event prediction with neural networks and Cox regression. *arXiv preprint arXiv:190700825*. 2019.
40. Katzman JL, Shaham U, Cloninger A, Bates J, Jiang T, Kluger Y. DeepSurv: personalized treatment recommender system using a Cox proportional hazards deep neural network. *BMC Med Res Methodol*. 2018;18(1):24.
41. Wu J, Chen X-Y, Zhang H, Xiong L-D, Lei H, Deng S-H. Hyperparameter optimization for machine learning models based on Bayesian optimization. *Journal of Electronic Science and Technology*. 2019;17(1):26–40.
42. Wu W, Li Y, Feng A, et al. Data mining in clinical big data: the frequently used databases, steps, and methodological models. *Military Medical Research*. 2021;8(1): 1–12.
43. Randall RL, Cable MG. Nominal nomograms and marginal margins: what is the law of the line? *Lancet Oncol*. 2016;17(5):554–556.
44. Li HB, Zhao FQ, Zhou J. Prognostic nomogram for disease-specific survival in patients with non-metastatic ampullary carcinoma after surgery. *Ann Surg Oncol*. 2019;26(4):1079–1085.
45. Taitt HE. Global trends and prostate cancer: a review of incidence, detection, and mortality as influenced by race, ethnicity, and geographic location. *Am J Men's Health*. 2018;12(6):1807–1823.
46. Walsh SM, Zabor EC, Stempel M, Morrow M, Gemignani ML. Does race predict survival for women with invasive breast cancer? *Cancer*. 2019;125(18):3139–3146.
47. de Geus SW, Sachs TE, Ng SCW, McAneny DB, Tseng JF. *Racial/ethnic Disparities in the Use of High-Volume Centers for Hepatobiliary and Pancreatic Cancer Surgery*. American Society of Clinical Oncology; 2019.
48. Vining CC, Schuitevoerder D, Turaga KK. Ampullary adenocarcinoma: the current state of adjuvant therapies. *Hepatobiliary Surg Nutr*. 2020;9(5):647–649.
49. Sineshaw HM, Ng K, Flanders WD, Brawley OW, Jemal A. Factors that contribute to differences in survival of black vs white patients with colorectal cancer. *Gastroenterology*. 2018;154(4):906–915.e907.
50. Gerend MA, Pai M. Social determinants of Black-White disparities in breast cancer mortality: a review. *Cancer Epidemiol Biomark Prev*. 2008;17(11):2913–2923.
51. Ward E, Halpern M, Schrag N, et al. Association of insurance with cancer care utilization and outcomes. *CA A Cancer J Clin*. 2008;58(1):9–31.
52. Buja A, Lago L, Lago S, Vinelli A, Zanardo C, Baldo V. Marital status and stage of cancer at diagnosis: a systematic review. *Eur J Cancer Care*. 2018;27(1), e12755.
53. Adler NE, Page AEK. The national academies collection: reports funded by national institutes of health. In: *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*. Washington (DC): National Academy of Sciences; 2008.
54. He C, Mao Y, Wang J, Huang X, Lin X, Li S. Surgical management of periampullary adenocarcinoma: defining an optimal prognostic lymph node stratification schema. *J Cancer*. 2018;9(9):1667–1679.
55. Yu H, Huang T, Feng B, Lyu J. Deep-learning model for predicting the survival of rectal adenocarcadinoma patients based on a surveillance, epidemiology, and end results analysis. *BMC Cancer*. 2022;22(1):210.
56. Jan B, Farman H, Khan M, et al. Deep learning in big data analytics: a comparative study. *Comput Electr Eng*. 2019;75:275–287.