A Nomogram for Individual Prediction of Poor Prognosis After Radical Surgery in Patients with Primary Pancreatic Duct Adenocarcinoma

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Source of support: This study was supported by grants from the Shanghai Anti-Cancer Association (EYAS PROJECT; no. SACA-CY1C19)

Background: Pancreatic cancer is a highly malignant tumor characterized by poor prognosis. TNM stage cannot always provide accurate prediction of prognosis, which is vital for individualized treatment. Therefore, a novel way to identify patients with poor prognosis after radical surgery is urgently needed.

Material/Methods: The nomogram was established based on a discovery cohort that included 554 patients with PDAC who had received radical surgery from 2012 to 2016. The clinicopathological data were collected. Poor prognosis was evaluated using 25 features, in which appropriate features for a prediction model were identified. A prediction model incorporating the selected features was established. The discriminative capacity was assessed by *C*-index, calibration by calibration plot, and clinical usefulness by decision curve. The bootstrapping approach was used to perform internal validation.

Results: Characteristics included in the nomogram were coronary artery disease and stroke history, elevated CA125, AJCC stage >II, R0 resection, operating time >6 h, poor differentiation, nerve invasion, length of stay >30 days, and postoperative complications. A C-index of 0.713 indicated good discrimination of the prediction model, and the calibration curve showed acceptable calibration. Survival analysis showed that this model had better discriminative capacity than the AJCC staging system and could distinguish relatively good prognosis from poor prognosis in patients at stage II (especially IIa) and IV.

Conclusions: Our study presents a valid and practical model to predict prognosis of pancreatic cancer patients, which contributes to individualized therapy by assisting surgeons to predict poor prognosis in patients who received radical surgery.

MeSH Keywords: Nomograms • Pancreatic Neoplasms • Prognosis

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/918882

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Background

Pancreatic cancer is one of the most lethal solid tumors, with extreme malignancy in the digestive system, which is the third most common cause of cancer-related death around the world [1,2]. Pancreatic duct adenocarcinoma (PDAC) accounts for more than 90% of all pancreatic cancer cases. The 5-year survival rate of pancreatic cancer remains less than 10% in the USA [3]. Accurate prediction of poor prognosis for patients with PDAC after radical surgery is of great significance and can influence treatment decisions. TNM stage has been widely accepted as a predictive parameter to indicate the prognosis of pancreatic cancer patients after radical surgery. However, TNM stage is determined mostly by anatomical features, which does not take the biological characteristics of the tumor into consideration. Previous studies have revealed several risk factors for pancreatic cancer, such as smoking, alcohol intake, obesity, and type 2 diabetes [4–7]. Although several publications have focused on the prognostic prediction of pancreatic cancer, most of these studies use data from the SEER database, which has a large sample size but limited clinicopathological parameters [8–10]. There are few studies focusing on resectable pancreatic cancer with a large sample size and abundant relevant information. Our study aimed to establish a valid and practical predicting nomogram that includes preoperative characteristics and clinicopathological features to predict the prognosis of patients with resectable PDAC.

Material and Methods

Patients

Research approval (No. 103 in 2019) was received from the local ethics committee of Ruijin Hospital affiliated to the School of Medicine, Shanghai Jiao Tong University. The ethics committee waived the need for informed consent because this was an observational retrospective study. Patients were recruited from Ruijin Hospital from 2012 to 2016. A complete assessment of medical records from the institutional database was conducted to select patients histologically diagnosed as PDAC who underwent radical surgery with curative intent. All patients were followed up until cancer-specific death, and those who died within 6 months after surgery were considered to have a poor prognosis.

The inclusion criteria were: 1) Patients with suspected pancreatic cancer between 18 and 80 years old and the tumor was evaluated as resectable or borderline resectable by a multidisciplinary team; 2) No absolute contraindications, and physical strength score ranging from 0 to 1; 3) Histopathologically confirmed as PDAC; 4) No secondary cancer or other malignant tumors; and 5) No chemoradiotherapy was performed

before surgery. The exclusion criteria were: 1) Loss to follow-up and incomplete data; 2) In-hospital death or death caused by postoperative complications within 1 month after surgery; and 3) Incomplete radical operation. Baseline clinicopathologic data, including age, sex, blood biochemical examination, tumor marker, and clinicopathological factors were obtained from medical records. For patients at stage IV with focal liver metastasis detected before surgery or newly-discovered single liver metastatic lesion discovered during surgery, radical surgery was performed if the patients or their relations insisted on surgical resection despite thorough explanation of the limited benefits of surgery.

Statistical analysis

R software was used to perform statistical analysis and visualize the results. Optimal features were selected by the least absolute shrinkage and selection operator (LASSO) method designed to reduce the dimensions of data [11,12]. Through LASSO regression, factors that were analyzed with nonzero coefficients were identified and selected [13]. The prediction model incorporating features selected using the LASSO regression model was established based on multivariable logistic regression analysis, which is used to assess the odds ratio (OR), 95% confidence interval (CI), and corresponding *P* value. All selected predictors with *P* value <0.05 were enrolled in the prediction model. The calibration of the model was assessed by calibration curves [14]. A *C*-index was generated to measure the discrimination capacity of the nomogram [15,16]. A validating *C*-index was generated from bootstrapping validation (1000 bootstrap resamples). Bootstrap resampling was performed by fitting the logistic model into a bootstrap sample, which was extracted from original sample [17]. The clinical usefulness of this nomogram was evaluated by decision curve analysis [18,19]. Area under the ROC curves (AUC) was also used to evaluate the discriminative capacity of the nomogram [20]. Risk score at 0.2–0.4 were considered as low risk, 0.4–0.7 as medium risk and 0.7–0.9 as high risk.

Results

Patients' characteristics

A total of 554 patients were included in the study. The discovery cohort consisted of 183 patients with poor prognosis (survival less than 6 months after radical surgery) and the control group included 371 patients with relatively good prognosis (survival longer than 6 months after radical surgery). There were 347 males and 207 females, with a mean age of 62.57±9.23 years (range 32–85 years). There were 343 cases of pancreaticoduodenectomy (PD), 210 cases of distal pancreatectomy (DP), and 1 case of total pancreatectomy (TP), all of which were

Table 1. Demographic and clinical characteristics of patients with resectable PDAC.

Demographic characteristics		Survival <6 months (%) (n=183)		Survival >6 months (%) (n=371)		Total (%) (n=554)	
Sex	Male	111	(60.66%)	236	(63.61%)	347	(62.64%)
	Female	72	(39.34%)	135	(36.39%)	207	(37.36%)
LOS	>30 days	41	(22.40%)	65	(17.52%)	106	(19.13%)
	≤30 days	142	(77.60%)	306	(82.48%)	448	(80.87%)
HTN	Yes	66	(36.07%)	126	(33.96%)	192	(34.66%)
	No	117	(63.93%)	245	(66.04%)	362	(65.34%)
CAD & stroke	Yes	18	(9.84%)	21	(5.66%)	39	(7.04%)
	No	165	(90.16%)	350	(94.34%)	515	(92.96%)
Anemia	Yes	90	(49.18%)	176	(47.44%)	266	(48.01%)
	No	93	(50.82%)	195	(52.56%)	288	(51.99%)
Jaundice	Yes	74	(40.44%)	163	(43.94%)	237	(42.78%)
	No	109	(59.56%)	208	(56.06%)	317	(57.22%)
Elevated fasting glucose	Yes	76	(41.53%)	154	(42.32%)	230	(41.52%)
	No	107	(58.47%)	217	(58.49%)	324	(58.48%)
Elevated CA125	Yes	52	(28.42%)	58	(15.63%)	110	(19.86%)
	No	131	(71.58%)	313	(84.37%)	444	(80.14%)
Elevated CA199	Yes	153	(83.61%)	289	(77.90%)	442	(79.78%)
	No	30	(16.39%)	82	(22.10%)	112	(20.22%)
R0 resection	Yes	141	(77.05%)	332	(89.49%)	473	(85.38%)
	No	42	(22.95%)	39	(10.51%)	81	(14.62%)
Smoking	Yes	39	(21.31%)	89	(23.99%)	128	(23.10%)
	No	144	(78.69%)	282	(76.01%)	426	(76.90%)
Alcohol intake	Yes	30	(16.39%)	54	(14.56%)	84	(15.16%)
	No	153	(83.61%)	317	(85.44%)	470	(84.84%)
ASA score	≥2	62	(33.88%)	109	(29.38%)	171	(30.87%)
	<2	121	(66.12%)	262	(70.62%)	383	(69.13%)
Vein resection	Yes	21	(11.48%)	36	(9.70%)	57	(10.29%)
	No	162	(88.52%)	335	(90.30%)	497	(89.71%)
Artery resection	Yes	9	(4.92%)	16	(4.31%)	25	(4.51%)
	No	174	(95.08%)	355	(95.69%)	529	(95.49%)
Poor differentiation	Yes	119	(65.03%)	211	(56.87%)	330	(59.57%)
	No	64	(34.97%)	160	(43.13%)	224	(40.43%)
Combined organ resection	Yes	19	(10.38%)	12	(3.23%)	31	(5.60%)
	No	164	(89.62%)	359	(96.77%)	523	(94.40%)

Table 1 continued. Demographic and clinical characteristics of patients with resectable PDAC.

Demographic characteristics		Survival <6 months (%) (n=183)		Survival >6 months (%) (n=371)		Total (%) (n=554)	
OT	>6 h	35	(19.13%)	49	(13.21%)	84	(15.16%)
	≤6 h	148	(80.87%)	322	(86.79%)	470	(84.84%)
Bleeding	>1000 ml	20	(10.93%)	25	(6.74%)	45	(8.12%)
	≤1000 ml	163	(89.07%)	346	(93.26%)	509	(91.88%)
Operative transfusion	Yes	109	(59.56%)	211	(56.87%)	320	(57.76%)
	No	74	(40.44%)	160	(43.13%)	234	(42.24%)
LNR	>0.2	46	(25.14%)	67	(18.06%)	113	(20.40%)
	≤0.2	137	(74.86%)	304	(81.94%)	441	(79.60%)
Nerve invasion	Yes	155	(84.70%)	282	(76.01%)	437	(78.88%)
	No	28	(15.30%)	89	(23.99%)	117	(21.12%)
AJCC stage	>II	64	(34.97%)	49	(13.21%)	113	(20.40%)
	≤II	119	(65.03%)	322	(86.79%)	441	(79.60%)
Clavien-Dindo grade	>1	26	(14.21%)	72	(19.41%)	98	(17.69%)
	≤1	157	(85.79%)	299	(80.59%)	456	(82.31%)

LOS – length of stay; HTN – hypertension; CAD – coronary artery disease; ASA – American Society of Anesthesiologists; OT – operating time; LNR – lymph node ratio; AJCC – American Joint Committee on Cancer.

performed according to tumor location combined with vascular reconstruction or dissection of lymph nodes. The demographic and clinicopathological variables of enrolled patients are summarized in Supplementary Table 1 and Table 1.

Feature selection

Of the demographic, laboratory examination, and clinicopathological variables, 9 potential predictors that had non-zero coefficients were identified and selected from 25 features (Figure 1A, 1B). The selected features were AJCC stage >II, coronary artery disease (CAD) and stroke history, elevated CA125, R0 resection, operating time (OT) >6 h, poor differentiation, nerve invasion, length of stay >30 days, and postoperative complications (Clavien-Dindo grade >1).

Establishment of prediction model

The coefficient value, OR with 95% CI, and P value of the 9 selected factors calculated by multivariate logistic regression model are listed in Table 2. A nomogram comprised of the factors above was established, which is presented in Figure 2. The specific points of each predictor are shown in Table 3.

Apparent performance of the nomogram to indicate poor prognosis

The calibration curve of the nomogram to predict poor prognosis in patients with resectable PDAC demonstrated good agreement in the discovery population (Figure 3A). A C-index of 0.713 with 95% CI ranging from 0.665 to 0.760 was generated. Through bootstrapping validation, the C-index was confirmed to be 0.689. Moreover, the AUC of the nomogram was 0.713 (95% CI 0.660–0.760) (Figure 3B). All of the above results suggested the good discriminative capacity of this model.

Clinical use of the nomogram

As shown in Figure 4, the decision curve suggested that if a patient and a doctor respectively showed a threshold probability of >17% and <73%, more benefit would be added than with the scheme when the nomogram was used to predict the prognosis of patients with PDAC. Moreover, based on this model to predict prognosis, net benefit was comparable with several overlaps within the range mentioned above.

Examples of the nomogram in use

Patient 1, 35 years old, had a tumor in the head of the pancreas with presence of jaundice. Preoperative and postoperative
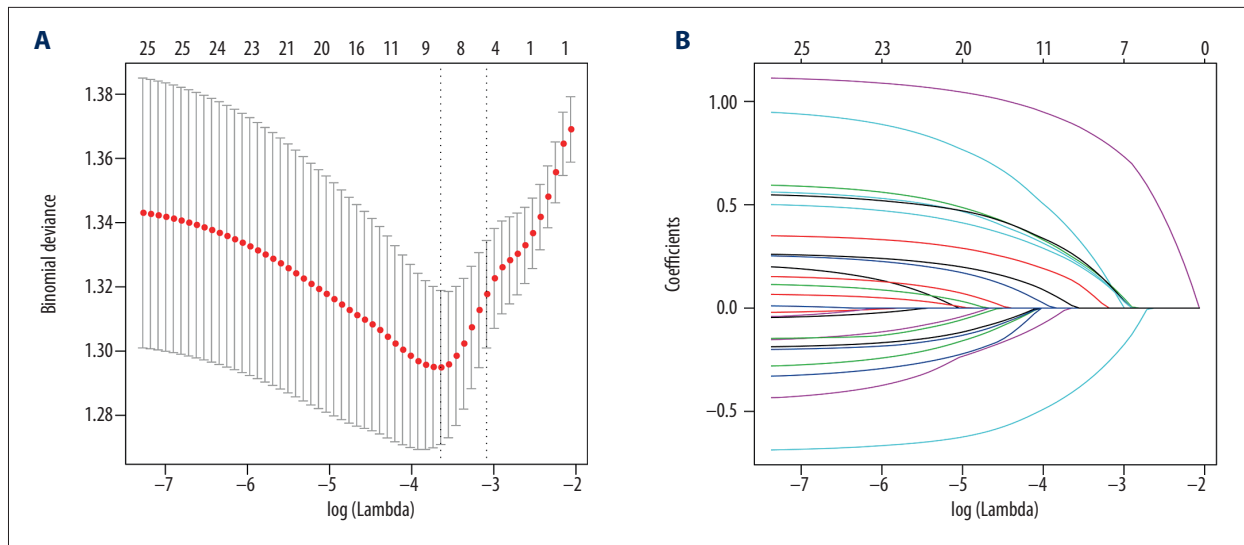
Figure 1. Clinicopathological parameter identification and selection by LASSO regression model. (**A**) Five-fold cross-validation was applied to select the most suitable parameter using LASSO regression model. (**B**) Coefficient curves of the 25 parameters. LASSO – the least absolute shrinkage and selection operator.

Table 2. Prediction factors for patients with poor prognosis after radical surgery.

Intercept and variable	β	Odds ratio (95% CI)	P value
Intercept	−0.9994067	0.3680978 (0.1755997–0.7583270)	0.00724
AJCC stage >II	1.0913924	2.9784183 (1.8147357–4.9552890)	1.96e−05
CAD & stroke history	0.8529103	2.3464659 (1.0777371–5.3129831)	0.03462
Elevated CA125	0.5128306	1.6700116 (1.0108799–2.7670180)	0.04535
R0 resection	−0.6917549	0.5006966 (0.2891940–0.8576446)	0.01234
OT >6 h	0.5332936	1.7045372 (1.0620359–2.7425817)	0.02727
Tumor grade low	1.6576758	1.6576758 (1.1017774–2.5077881)	0.01586
Nerve invasion	0.4715138	1.6024181 (0.9678093–2.6965005)	0.07045
LOS >30 days	0.3441662	1.4108131 (0.8400952–2.3675593)	0.19174
Clavien-Dindo grade >1	1.3185691	1.3185691 (0.6981923–2.4884413)	0.39198

* *P*<0.05 was considered to denote statistical significance. AJCC – American Joint Committee on Cancer; CAD – coronary artery disease; OT – operating time; LOS – length of stay.

imaging examinations are shown in Figure 5A–5D. The details of the predicted risk factors of this patient are presented in Figure 5E. The risk of poor prognosis predicted by the nomogram was more than 75%. Moreover, this patient developed liver metastasis 1 month after radical surgery and died 80 days later.

Patient 2, aged 51 years, had a tumor located in the body of the pancreas, with presence of abdominal pain. Preoperative and postoperative imaging examinations are shown in Figure 6A–6D. The details of the predicted risk factors of this patient are shown in Figure 6E. The risk of poor prognosis determined by the

nomogram was more than 60%. Unfortunately, although the patient's AJCC stage was II, he developed multiple liver metastasis 2 months after radical surgery and died 111 days later.

Kaplan-Meier curve analysis

TNM stage is currently used to predict the prognosis of cancer patients. According to the 8th edition AJCC staging system, we plotted survival curves stratified by different stages (Figure 7A). The result showed that patients at stage I compared with those at stage II showed no obvious difference in long-term survival (*P*=0.1458), almost the same as patients at stage II with
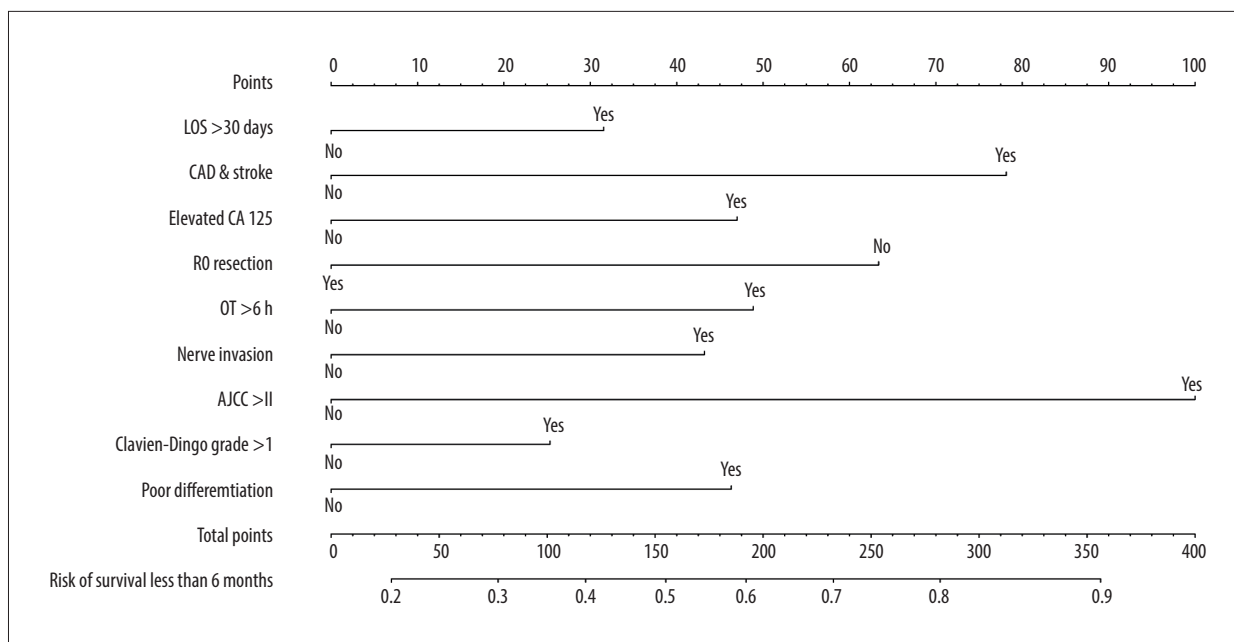
Figure 2. Developed of a nomogram to predict poor prognosis. The nomogram was established based on the discovery cohort, with the use of LOS >30 days, CAD and stroke history, elevated CA125, R0 resection, OT >6 h, nerve invasion, AJCC stage >II, complications Clavien-Dindo grade >1, and poor differentiation. LOS – length of stay; CAD – coronary artery disease; OT – operating time; AJCC – American Joint Committee on Cancer.

Table 3. Points of each predictor.

Variable	Status	Points
LOS >30 days	No	0
	Yes	32
CAD & stroke history	No	0
	Yes	78
Elevated CA125	No	0
	Yes	47
R0 resection	No	63
	Yes	0
OT >6 h	No	0
	Yes	49

Variable	Status	Points
Nerve invasion	No	0
	Yes	43
AJCC stage >II	No	0
	Yes	100
Complications (Clavien-Dindo grade >1)	No	0
	Yes	25
Poor differentiation	No	0
	Yes	46

LOS – length of stay; CAD – coronary artery disease; OT – operating time; AJCC – American Joint Committee on Cancer.

stage III (P=0.0364). However, when stratified by risk group determined by our model, the survival curves showed good discrimination ($P_{low-medium}$=0.0007, $P_{medium-high}$<0.0001) (Figure 7B). Moreover, when we applied our model in patients at different stages, we found the model showed good discriminative capacity of survival in patients at stage II ($P_{low-medium}$=0.0120, $P_{medium-high}$<0.0051) and stage IV (P=0.0137) (Figure 7C–7F). To investigate the specific population that could potentially benefit from this model, we performed further subgroup analysis using patients at stage II. As shown in Figure 7G and 7H,

the model showed excellent discrimination in patients at stage IIa ($P_{low-medium}$=0.0046, $P_{medium-high}$<0.0007), but not in patients at stage IIb.

Discussion

Recently, using nomograms to predict prognosis or other endpoints has drawn increasing attention in oncologic research. A reliable prediction model based on well-selected risk factors
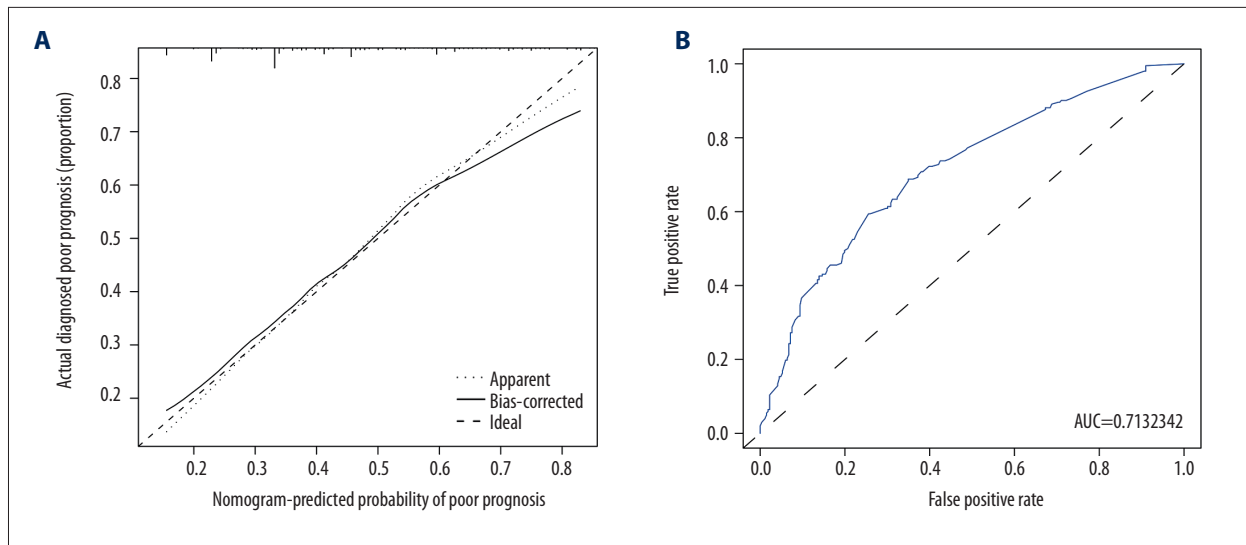
Figure 3. Calibration and ROC curve of the poor prognosis prediction. (**A**) Calibration curves. The predicted possibility of poor prognosis is indicated by the x axis and the actual possibility of poor prognosis is indicated by the y axis. (**B**) ROC curves. The x axis represents the false-positive rate, while the y axis shows the true-positive rate. AUC – the area under ROC curve.
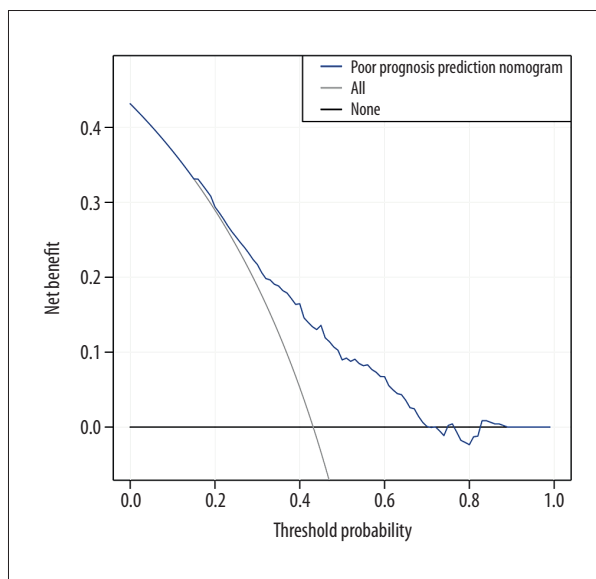

Figure 4. Clinical usefulness of the poor prognosis prediction nomogram. The y axis represents net benefit. The x axis shows threshold probability. The blue line displays the benefit of our nomogram. The gray line suggests that all patients have poor prognosis, while the black line indicates that no patient has poor prognosis.

can increase the accuracy of prediction and contribute to clinical decision-making [21–25]. In the present study, we established and validated a practical prediction model to predict the prognosis of patients with PDAC after radical surgery, using 9 easily available variables, including AJCC stage >II, CAD and stroke history, elevated CA125, R0 resection, operating time >6 hr poor differentiation, nerve invasion, length of

stay >30 days, and postoperative complications (Clavien-Dindo grade >1). The discovery cohort indicated the good discrimination and calibration of the prediction model, with a C-index of 0.713. Similarly, internal bootstrapping validation also suggested acceptable discriminative ability, with a C-index of 0.689. Survival analysis showed that this model had better discriminative capacity than the AJCC staging system and could distinguish relatively good prognosis from poor prognosis in patients at stage II (especially IIa) and IV. These results suggest that this model is a valid and practical model to predict the prognosis of pancreatic cancer patients, and can potentially contribute to individualized therapy by assisting surgeons to identify those patients with poor prognosis or patients who cannot benefit from radical surgery

The classic clinicopathological characteristics used in this nomogram, such as AJCC stage >II, R0 resection, poor differentiation, and nerve invasion, are in line with previous studies [26–29]. The importance of R0 resection for pancreatic surgery is widely acknowledged. In accordance with previously published cohort studies, tumor differentiation was recognized as an independent prognostic factor by multivariate Cox regression analysis for patients with PDAC and also for patients with periampullary after radical surgery [30–32]. A previous retrospective study using data from the SEER database suggested that with tumor differentiation included into the AJCC staging system, the present evaluation approach can offer a better survival prognostication [33]. Pancreatic cancer is neurotropic, which leads to postoperative recurrence. Perineural invasion (PNI), which may be related to tumor recurrence, has also been reported to independently predict prognosis [34]. This could be precisely confirmed by our examples mentioned above.
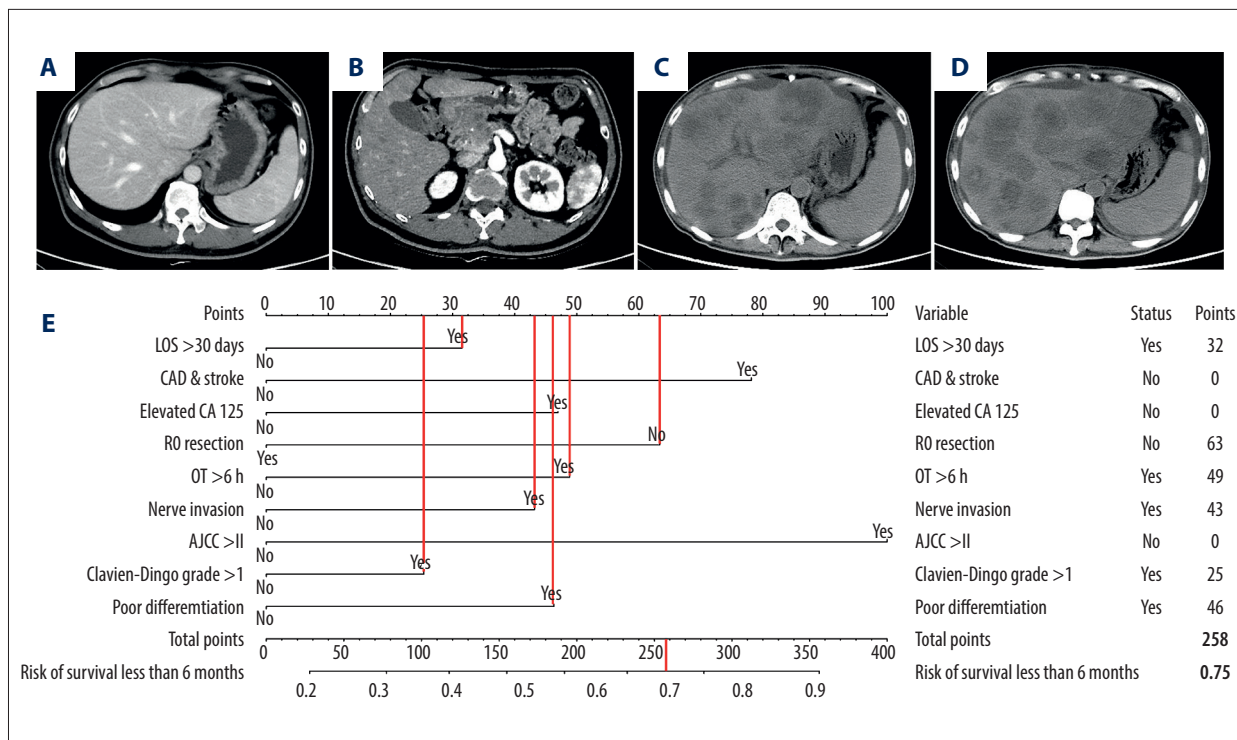
Figure 5. An example of the nomogram in use. (**A–D**) Preoperative and postoperative imaging examinations. (**E**) Details of the predicted risk factors.
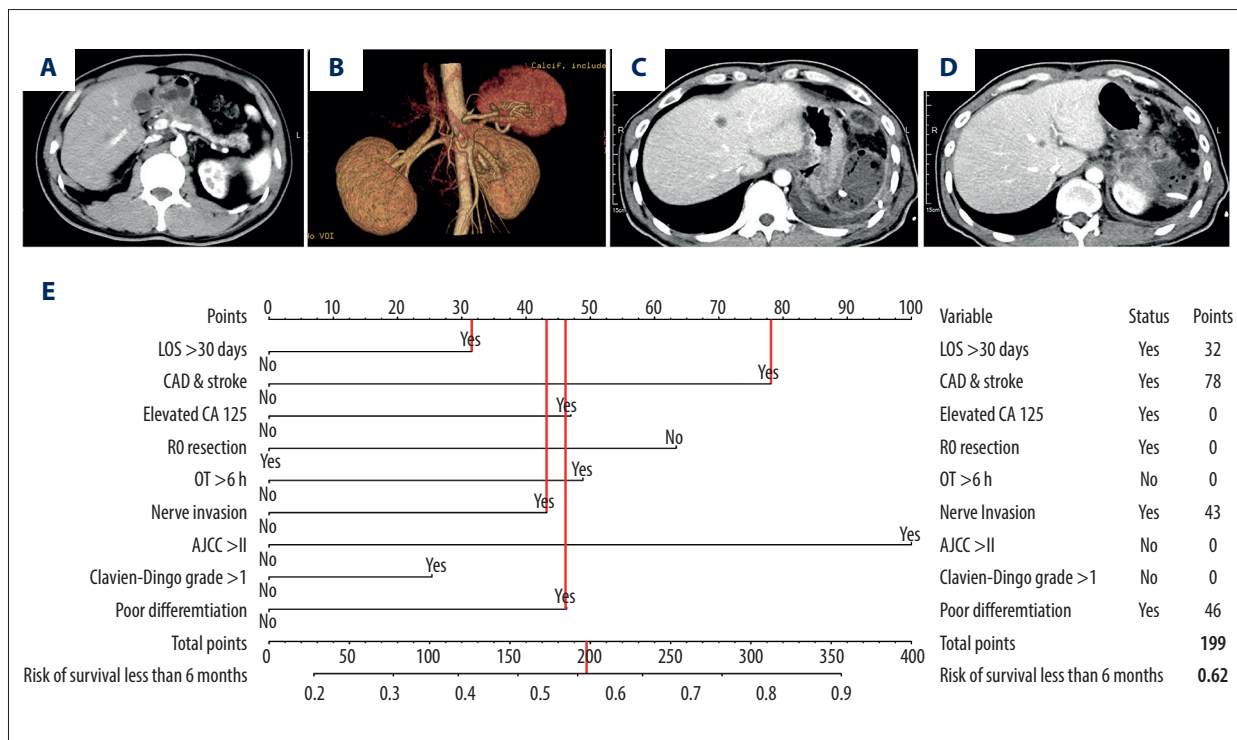

Figure 6. Another example of nomogram in use. (**A–D**) Preoperative and postoperative imaging examinations. (**E**) Details of the predicted risk factors.
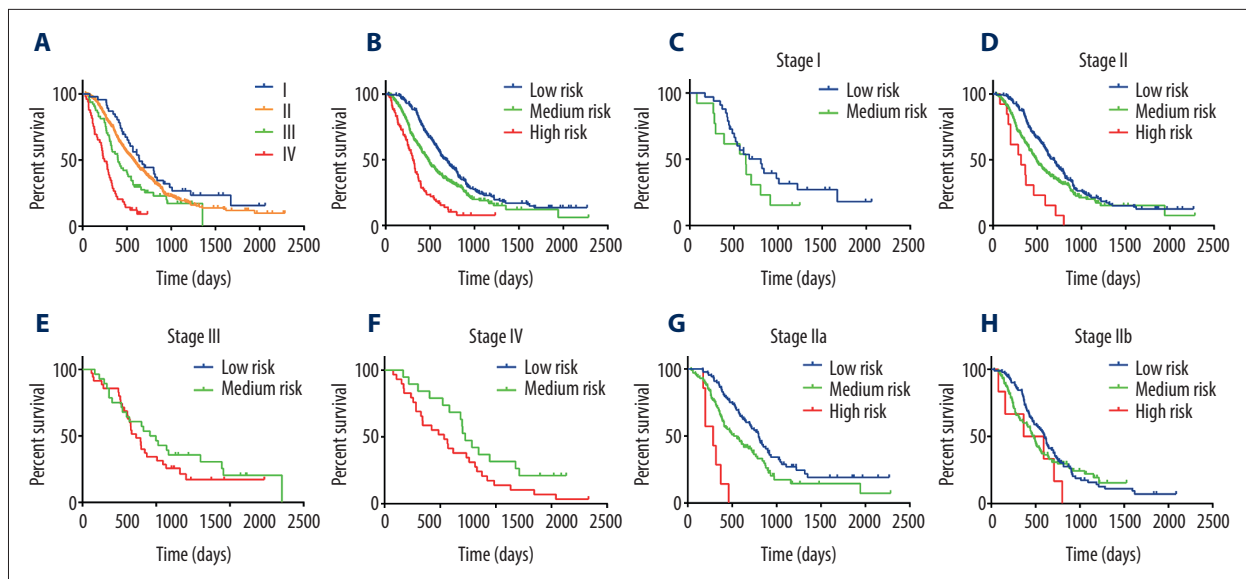
Figure 7. Kaplan-Meier curve analysis. Survival curves stratified by (**A**) AJCC stages and (**B**) risk groups defined by the prediction model. (**C–F**) Survival curves stratified by risk groups in patients at stage I, II, III, and IV. (**G–H**) Survival curves of patients at stage IIa and IIb stratified by risk groups.

Postoperative pathology showed perineural invasion in both patients, and metastasis eventually occurred in both patients within a short period.

Gastrointestinal malignancy, especially pancreatic cancer, is usually associated with chronic diseases such as coronary heart disease, stroke, and cerebral infarction. Advanced age is a high-risk factor for pancreatic cancer itself, and elderly patients usually also have coronary heart disease and cerebral infarction. It has been reported that chronic diseases such as diabetes are often associated with poor prognosis of pancreatic cancer [35]. In addition, patients with a history of coronary heart disease or cerebral infarction are generally in worse physical condition, which may result in worse prognosis.

Many studies on CA125 have been not only clinically relevant but also inseparable from basic research [36–38]. A Chinese team specifically conducted a series of studies on CA125 to clarify its important role in clinical practice, as well as prediction of resectability and prognosis [39–41]. Increased CA125 often indicates a high tumor burden and high degree of malignancy. A nomogram established by He et al. [32] to predict individual risk of OS and PFS in patients with periampullary adenocarcinoma after pancreatoduodenectomy included LNR as a significant predictor, which was confirmed by a recent study using SEER database to predict disease-specific survival in patients with non-metastatic ampullary carcinoma [42]. However, LNR was not incorporated into our prediction model due to the different tumor type, the larger cohort in our study, and different statistical approach. Notably, more than 6 h of operating time, more than 1 month stay in hospital, and more

severe complications (Clavien-Dindo Grade >1) tend to indicate complicated surgery [43–46], and the complexity of surgery is often positively associated with tumor malignancy. Most malignant tumors can invade the important organs and blood vessels nearby, which greatly increases the difficulty of surgery and worsens the prognosis.

Two patients were selected to test the clinical usefulness of our model. The predicted possibility of poor prognosis of these 2 people were 0.75 and 0.62. Notably, these 2 patients, classified as AJCC less than stage III, which is conventionally considered to have a positive prognosis, had a poor prognosis, with 80 and 136 days of postoperative survival, indicating that additional clinicopathological parameters beyond AJCC stage should be taken into consideration when determining patient prognosis. This is why we established this prediction model with more risk factors included. In addition, this model showed good discriminative ability when applied to patients at stage II and stage IV (Figure 7D, 7F). Conventionally, stage IV with liver metastasis is definitely a contraindication of radical surgery. However, our results suggested that patients at stage IV could benefit from radical surgery, which is in accordance with some previous studies [47,48]. Interestingly, a similar result was also observed in a recently published international population-based study using the SEER database, suggesting that patients at stage III or IV with surgical resection showed higher survival estimates [49]. Therefore, through this prediction model, we can identify patients at stage IV who are more likely to have a poor prognosis. This group of patients should be asked to participate in clinical trials for possible improvement. For patients with medium risk, the prognosis has

been significantly improved, with a medium survival time of more than 300 days. Through subgroup analysis of patients at stage II, our model showed good discrimination in stage IIa but not in stage IIb, possibly because patients at stage IIb are accompanied by lymphatic metastasis, and the required positive rate and examined number of lymph nodes remain controversial [50,51]. Moreover, the AJCC staging system needs to be specified and updated [52].

Our study has certain limitations that must be considered. Firstly, genomic characteristics of patients were not included into the nomogram [53,54], and precision medicine is becoming increasingly important in tumor treatment. Secondly, this was a retrospective study based on clinical data from a single center; therefore, selection bias was inevitable. Thirdly, we did not include all potential factors related to prognosis into the risk factor selection procedure because some possible characteristics were not completely recorded, such as family financial situation, patient compliance, and other conditions. Notably, adjuvant therapy is an important prognostic factor [55], but

we did not include this predictor into our nomogram owing to the limited use of chemotherapy in our center, which could lead to biased conclusions. We will collect more patient cases receiving adjuvant chemotherapy in the future to perform further analysis. Finally, although our nomogram was robust, with extensive internal validation using bootstrap testing, external validation is still required. In the future, we plan to conduct prospective experiments and use data from other centers to further validate the discriminative capacity of this nomogram.

Conclusions

Our study establishes a valid and practical nomogram using easily available characteristics, which contributes to individualized treatment by assisting surgeons to identify patients at different stages who received radical surgery with poor prognosis. However, external validation to further verify the nomogram is required.

Supplementary Data

Supplementary Table 1. Demographic and clinicopathologic characteristics of the enrolled patients.

Variable	Number (n=554)		Variable	Number (n=554)	
Age	63	(57, 69)	**Venous invasion**	127	(22.90%)
Sex (Male)	359	(64.82%)	**Neural invasion**	437	(78.78%)
Past history			**Surgical procedure**		
Hypertension	192	(34.61%)	PD	343	(61.91%)
Cardio-cerebrovascular disease	39	(7.04%)	DP	210	(37.91%)
Clinical manifestation			TP	1	(0.18%)
No symptoms	51	(9.21%)	**R0 resection**	473	(85.40%)
Jaundice	237	(42.78%)	**Examined lymph nodes**	12	(0, 48)
Anemia	266	(48.01%)	**Positive lymph nodes**	0	(0, 14)
Laboratory tests			**LNR**	0.028	(0, 0.186)
Fasting glucose (mmol/L)	5.9	(5.2, 7.1)	**T stage**		
CA125 (u/ml)	16.9	(10.2, 28.9)	T1	95	(17.15%)
CA19-9 (u/ml)	176.4	(52.7, 560.2)	T2	289	(52.17%)
CEA (ng/ml)	3.7	(2.3, 8.1)	T3	90	(16.25%)
Tumor location			T4	80	(14.44%)
Pancreatic head	330	(59.63%)	**N stage**		
Pancreatic body/tail	224	(40.37%)	N0	296	(53.43%)
Tumor size (cm)	3	(2.5, 4)	N1	207	(37.36%)
Arterial invasion	70	(12.68%)	N2	51	(9.21%)

Variable	Number (n=554)		Variable	Number (n=554)
M stage			**Adjuvent chemotherapy (n=207)**	
M0	503 (90.79%)		GEMOX	99 (47.83%)
M1	51 (9.21%)		GEM	55 (26.57%)
Tumor differentiation			S1	29 (14.01%)
Poor	330 (59.57%)		AG	15 (7.25%)
Moderate/ well	224 (40.43%)		GS	9 (4.35%)

PD – pancreaticoduodenectomy; DP – distal pancreatectomy; TP – total pancreatectomy.

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